THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. XXVII FEBRUARY, 1932 No. 2

MENSURATION OF THE HEART AND CHEST IN THE LEFT POSTEROANTERIOR OBLIQUE POSITION A COMPARATIVE STUDY

I. RELATION OF THE TRANSVERSE DIAMETER OF THE HEART TO THE THORAX*

By WALTER W. FRAY, M.S., M.D.
ROCHESTER, NEW YORK

THE posteroanterior position has been used chiefly in the past to establish correlations between the heart and thorax. While the left oblique view has been used for a long time to determine the configuration of the cardiac shadow (Vaquez and Bordet[10]) and more recently to determine the diameter of the aorta and transverse diameter of the heart (O'Kane, Andrew, and Warren[8]) (Hampton and Jones[6]), I am familiar with no work correlating the cardiovascular shadow in the left oblique view with the chest cage, thus permitting comparative mensuration of the two. Owing to the great variation in size, weight, height, etc., of different individuals, the actual size of the cardiovascular shadow is of importance only when it becomes evident that it is abnormal for that particular individual. It was, of course, the recognition of this fact which led to the compilations on cardiac mensuration in the posteroanterior view by Claytor and Merrill,[3] Van Zwaluwenburg and Warren,[9] Kreuzfuchs,[7] Bardeen,[1] Eyster,[5] and others.

The cardiovascular shadow in the left anterior oblique position has been studied with much interest in this clinic for many years in an attempt (1) to define the topographical relations of the heart to the surrounding structures and to identify the anatomical parts silhouetted, (2) to establish definite criteria by means of which normal and diseased organs may be differentiated.

The data presented in this series of papers represent a further elaboration of this study and deal specifically with comparative mensuration of the heart and great vessels in relation to the thorax. Correlations relating to the left oblique view may be conveniently grouped for purposes of study as follows: (*a*) correlation of the cardiac measurements with the thorax in the left oblique position, (*b*) correlation of the measurements of the aortic arch shadow with the thorax in the left oblique position, (*c*) correlation of the diameters of the cardiovascular shadow in the left oblique position with those of the posteroanterior position. The present paper will be concerned with the first of these and more specifically will relate to comparative mensuration of the transverse diameter of the heart and the chest cage.

* From the Division of Radiology of the Department of Medicine of the University of Rochester, School of Medicine and Dentistry and the Strong Memorial Hospital, Rochester, N. Y.

METHOD

Anatomical Considerations. A preliminary study of cross sections of the human body at the cardiac and aortic arch levels was made, projecting these at varying angles in the left oblique position to aid in establishing general relationships. It was realized that these projections gave only general information, but they served as a basis or starting point for the rest of the work. Angles of rotation of 35°, 45°, 60°, and 66° were used. The range of the angles was adequate to give working clues upon which to base the measurements.

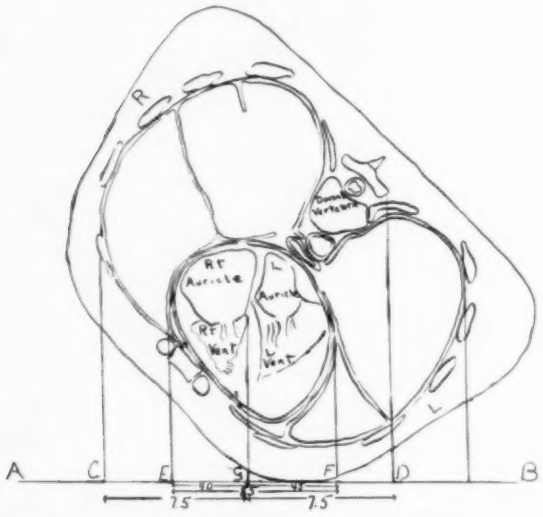


Fig. 1. Cross section of chest at cardiac level rotated 45° to base line. Note that the interventricular septum when projected is equidistant from the projected right axillary margin and the left costovertebral articulations. (Adapted from Eyclesheymer and Schoemaker.)

An examination of the cross section of the heart projected at a 45° angle revealed the most useful information. At this angle (Fig. 1) the interventricular septum is approximately at right angles to the base line, AB. This septum divides the heart into two nearly equal portions. The left ventricle is slightly larger than the right due to its heavier muscular layer. The interventricular septum (G) is equidistant (7.5 cm.) from the projected right anterior axillary chest wall (C) and the projected left costovertebral articulations (D) at this level. In other words, the projected septum is midway between these two points which are easily obtained on any 45° left oblique film, and if these two points are known it should be possible to interpolate the third (the septum) with reasonable accuracy.

The transverse diameter of the heart (EF) in this position is slightly more than one-half the distance between the projected points (CD) of the right anterior chest wall and the left costovertebral articulations (15.0 cm.). This appears to be due, however, to the high transverse position which the heart assumes after death, and this condition does not obtain in the average chest during life, as will be demonstrated later by accurate mensuration of the heart and chest teleroentgenographically in the living subject. The heart rotates about its vertical axis (clockwise) as it ascends in the thorax, and therefore an angle of approximately 40° rather than 45° was used in obtaining many of the films for this study. Angles less than 40° and more than 45° will result in a rotation of the interventricular septum away from the direction of the axis of the primary beam of radiation except in the extreme hyposthenic or hypesthenic types of individual.

While the preliminary studies were of aid in obtaining general information, it is apparent that these cross sections may not portray relationships accurately. At death, the diaphragms relax, the heart rises in the thorax, and the latter may be flattened or deformed by pressure. An accurate check, however, can be made on these relationships by comparing the findings of left oblique projection obtained during life with the actual anatomical findings of the heart and aorta at autopsy, i.e., hypertrophy and dilatation of the various chambers of the heart, pericardial effusion, etc. This furnishes indisputable evidence of the accuracy of the deductions from the left oblique film.

In this way we established our normal, supplementing the series with similar studies of patients still living, who by history, symptoms, and signs, gave no indication of

cardiovascular disease. No case of definite or doubtful disease relating to the heart or great vessels was included in this normal series, and all cases of the pathological group were autopsied.

The attempt was made in each case to obtain the left oblique view at an approximate angle of 45°, i.e., such an angle that the plane of the interventricular septum would fall in line with the axis of the primary beam of radiation. This would permit correlations later of the size of the two ventricles with the thorax and would afford an opportunity to recognize a disproportion in size of either ventricle.

Cases which were overrotated or rotated insufficiently were eliminated from the series. It became important to recognize such cases. This was done by noting the relative position of the spine in relation to the margins of the rib cage. It is apparent that in the usual posteroanterior view, the spine will be midway between the two sides of the chest cage (if the chest is not deformed) and in the lateral view, with the chest rotated 90°, the spine will be noted at the extreme posterior boundary of the thorax. Positions between these if the chest is symmetrical will show the spine changing its relative position according to the degree of rotation. From experience, it was found that satisfactory films were obtained when the diameter of the chest to the right of the spine was approximately twice as great as that to the left (ratio 2 to 1). With few exceptions, the variation of this ratio in the entire series of 75 cases was between the limits of 1.8 and 2.2. This rule was found a simple one to apply in making a preliminary survey of a film to decide if the degree of rotation came within proper limits.

A preliminary roentgenoscopy is of material aid in determining the correct position of the patient for the left oblique film. The degree of rotation of the patient is varied until the minimum transverse diameter of the heart is obtained. The long axis of the heart now runs roughly parallel with the spine, and the position is satisfactory for exposure of the film. Usually the projected left ventricle comes close to or overlies the spine slightly if the heart is normal and emphysema is absent. The projected right ventricular contour is nearer the right axillary wall than the projected left ventricular contour is to the left chest wall in normal cases. The main criteria for this position, however, are the minimum transverse diameter of the heart and the direction of the long axis of the heart.

A total of 75 cases have been studied in both the posteroanterior and left oblique positions. Forty of these represent autopsied cases, the cardiac pathology of which is known. Thirty-five cases were selected because they showed no evidence of cardiac pathology and were admitted to the hospital for other reasons (not relating to the cardiovascular system) and as stated above were used by us in order to supplement the normal series. The ages varied from four to seventy-three years. There were 34 females and 41 males in the series.

RESULTS

On correlating the transverse diameter of the heart with the thorax, the measurement of the transverse diameter of the chest from the right lateral chest wall to the left costovertebral articulations was found to be most valuable.

It was noted that in most instances the transverse diameter of the heart fell in two groups: a normal group in which the transverse diameter was less than one-half the diameter of the chest, measured from the right lateral chest wall to the left costovertebral articulations, and a group in which one or both of the ventricles were enlarged, and in which the transverse diameter of the heart exceeded one-half this same diameter of the chest.

Table 1 lists the findings regarding this correlation in 42 normal hearts. When the chest measurement (from the right anterior chest wall to the left costovertebral articulations) is divided by the transverse diameter of the heart in the oblique view, an average of 2.02 for the group is ob-

TABLE I

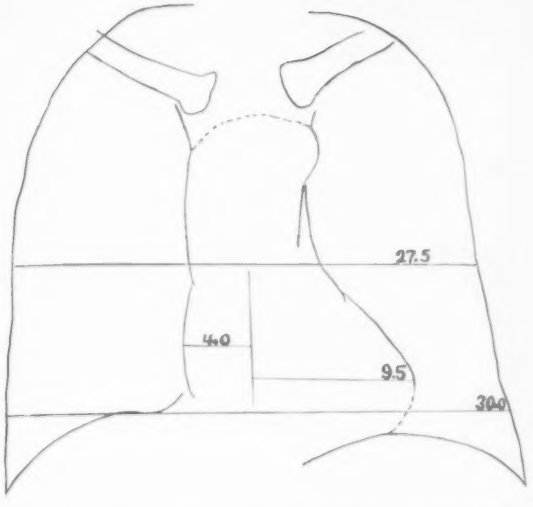
NORMAL HEARTS

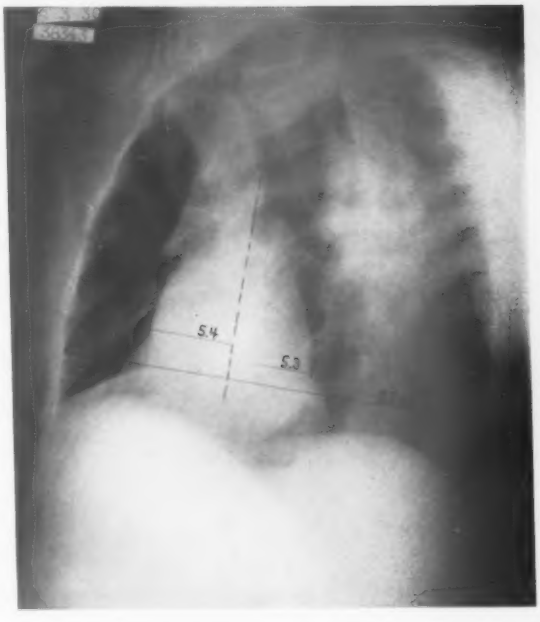
Correlation of the Transverse Diameter of the Heart with the Chest

Case	Age	Index of Rotation	O.T.D.*	O.C.S.†	O.C.S./O.T.D.	Pathological Findings	
						Heart Size	Heart Weight
			cm.	cm.			grams
H.S.	68		10.4	20.5	2.0	Brown atrophy No enlargement	
I.H.	59	2.0	10.7	22.2	2.1	No enlargement	380
L.H.	72	2.2	11.2	22.5	2.0	Brown atrophy No enlargement	260
M.K.	54	2.2	10.8	21.4	2.0	No enlargement	330
E.P.	37	2.1	12.0	19.4	1.6	Extremely obese heart No hypertrophy	300
N.F.	43	2.0	12.6	23.6	1.9	No enlargement	300
I.F.	64	2.1	12.2	23.0	1.9	No enlargement	350
						Clinical Findings	
D.M.	25	2.2	8.2	17.8	2.2	No evidence of cardiac disease	
N.S.	15	2.0	8.2	16.9	2.0	No evidence of cardiac disease	
I.W.	19	1.9	10.6	19.0	1.9	No evidence of cardiac disease	
E.B.	50	2.4	10.0	18.0	1.3	No evidence of cardiac disease	
D.C.	40	1.9	9.2	20.1	2.3	No evidence of cardiac disease	
F.G.	49	2.0	10.2	20.0	1.9	No evidence of cardiac disease	
R.C.	26	2.2	8.9	19.4	2.2	No evidence of cardiac disease	
L.M.	15	2.1	8.3	18.0	2.2	No evidence of cardiac disease	
V.W.	16	1.8	7.5	17.3	2.2	No evidence of cardiac disease	
L.W.	27	1.8	10.1	19.5	1.9	No evidence of cardiac disease	
P.A.	45	2.0	11.1	19.7	1.8	No evidence of cardiac disease	
A.P.	37	1.9	9.2	18.4	2.0	No evidence of cardiac disease	
C.M.	24	1.9	8.9	18.4	2.1	No evidence of cardiac disease	
L.B.	16	2.2	8.8	19.8	2.2	No evidence of cardiac disease	
R.B.	53	1.9	11.1	21.2	1.9	No evidence of cardiac disease	
M.H.	48	2.0	10.4	18.5	1.8	No evidence of cardiac disease	
A.C.	20	2.0	11.3	20.8	1.9	No evidence of cardiac disease	
I.L.	29	1.9	10.1	18.3	1.8	No evidence of cardiac disease	
M.W.	8	1.8	6.9	15.2	2.2	No evidence of cardiac disease	
M.S.	22	2.2	9.0	17.6	2.0	No evidence of cardiac disease	
E.H.	39	1.8	10.1	20.0	2.0	No evidence of cardiac disease	
C.T.	17	2.1	9.5	20.2	2.1	No evidence of cardiac disease	
S.M.	40	1.8	9.3	18.4	2.0	No evidence of cardiac disease	
E.B.	34	2.0	9.3	20.0	2.2	No evidence of cardiac disease	
G.F.	56	1.9	11.0	20.5	1.9	No evidence of cardiac disease	
F.R.	43	2.1	10.1	20.6	2.0	No evidence of cardiac disease	
L.H.	23	2.0	8.7	18.6	2.1	No evidence of cardiac disease	
M.L.	22	1.9	8.5	17.5	2.0	No evidence of cardiac disease	
L.H.	44	2.1	8.9	17.5	2.0	No evidence of cardiac disease	
P.B.	38	2.2	8.3	19.1	2.3	No evidence of cardiac disease	
M.H.	16	1.9	8.8	17.0	1.9	No evidence of cardiac disease	
M.J.	24	2.2	7.8	17.0	2.2	No evidence of cardiac disease	
R.T.	22	1.7	8.8	18.5	2.1	No evidence of cardiac disease	
A.M.	11	1.7	7.4	16.5	2.2	No evidence of cardiac disease	
B.G.	54	2.2	9.0	21.0	2.3	No evidence of cardiac disease	
Total 42					Av. Index 2.02		

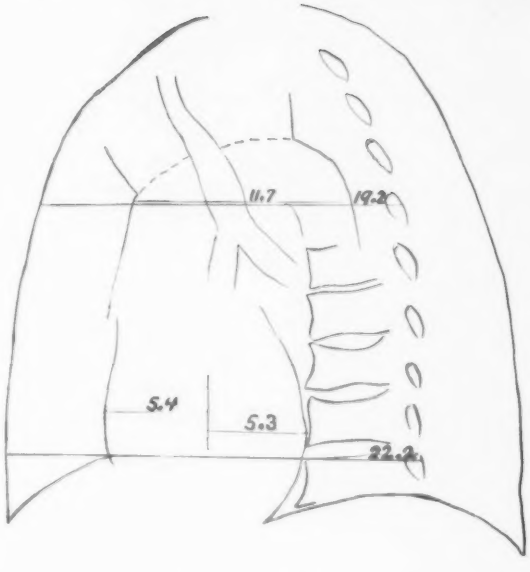
* O.T.D.—Oblique transverse diameter of heart.

† O.C.S.—Chest diameter from right axillary chest wall to left costovertebral articulation.





FIGS. 2, 3 and 4. Heart of normal size. Left oblique film with tracings of both posteroanterior and left oblique films. The transverse diameter of the heart (10.7 cm.) in the oblique view is approximately one-half the chest diameter from the right axillary region to the left costovertebral articulation (22.0 cm.). Note the rather symmetrical appearance of the normal heart in this view. The heart at autopsy showed no evidence of either dilatation or hypertrophy. The manner in which the position of the interventricular septum is determined and the measurements are made at the aortic arch will be described in a subsequent communication.



tained. The highest figure obtained was 2.3 (3 cases). Only one case was noted below 1.8. In this case, the heart was not hypertrophied at autopsy, but an extremely obese heart was noted. Thirty-four out of 42 cases showed an index of 1.9–2.2 inclusive. The age period for this normal group was eight to seventy-two years.

Figures 2, 3, and 4 show the measurements of the left oblique film and the tracings of the heart of a man of fifty-nine years. A heart of normal size (weight 380 grams) was found at autopsy a short time after this film was obtained. The transverse diameter of this heart in the oblique position is 10.7 cm., which is approximately one-half the projected chest diameter from the right axillary region to the left costovertebral articulations (22.0).

Table II lists the findings in similar fashion of 24 cases which showed (at postmortem) an enlargement of both sides of the heart. The highest index obtained in this series was 1.7 (one case) and the lowest 1.2 with an average of 1.42. The weight of the hearts at autopsy varied from 150 grams in a child of seven years to a maximum of 920 grams in a sixty-five year old adult. Most of these hearts were described by the pathologist as markedly or extremely hypertrophied or dilated. There were 5 cases in which ventricular hypertrophy was slight.

The chest of a patient who showed a pro-

TABLE II

PATHOLOGICAL HEARTS—BILATERAL ENLARGEMENT

Correlation of Transverse Diameter with Chest

Case	Age	Index of Rotation	O.T.D.*	O.C.S.†	O.C.S./O.T.D.	Pathological Findings	
						Heart Size	Heart Weight
			cm.	cm.			grams
G.H.	50	2.0	15.5	20.5	1.5	Pronounced enlargement	560
S.M.	15	2.0	11.9	19.5	1.6	Extreme enlargement	640
B.D.	20		11.6	16.4	1.4‡	Slight enlargement	305
A.V.	57	2.3	15.5	19.5	1.3	Pronounced enlargement	580
F.V.	69	1.8	16.1	22.8	1.4	Pronounced enlargement	660
C.D.	51	1.7	14.5	22.5	1.6	Slight enlargement	340
S.H.	65	2.3	16.8	24.0	1.4	Extreme enlargement	920
F.O.	46	1.9	15.9	24.4	1.5	Pronounced enlargement	640
I.S.	37	2.2	14.5	21.0	1.4	Extreme enlargement	900
J.S.	72	1.8	13.7	19.6	1.4	Moderate enlargement	480
F.S.	43	2.1	14.6	21.2	1.4	Slight enlargement	430
C.D.	71	2.3	15.0	23.3	1.5	Pronounced enlargement	670
J.P.	42	2.5	16.0	21.5	1.3§	Slight enlargement	425
H.B.	60	1.7	16.5	20.5	1.2	Pronounced enlargement	800
J.S.	41	2.2	18.8	22.5	1.2	Extreme enlargement	800
C.P.	71	1.9	15.7	22.9	1.5	Pronounced enlargement	700
G.K.	65	2.2	14.7	21.5	1.5	Moderate enlargement	480
C.S.	63	2.1	14.3	21.5	1.5	Moderate enlargement	480
E.C.	50		14.5	21.3	1.4	Pronounced enlargement	610
S.B.	7	1.7	8.5	15.8	1.7	Slight enlargement	150
T.P.	49	2.5	14.4	23.0	1.6	Pronounced enlargement	710
L.J.	4	2.2	9.5	14.0	1.5	Moderate enlargement	225
R.B.	59	1.7	18.5	22.0	1.2	Extreme enlargement	600
E.H.	76	2.1	13.6	19.0	1.4	Pronounced enlargement	602
Total 24					Av. Index 1.42		

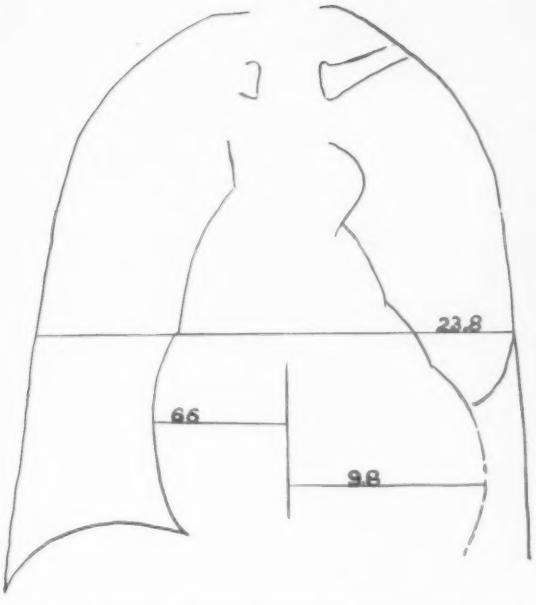
* O.T.D.—Oblique transverse diameter of heart.
† O.C.S.—Chest diameter from right axillary chest wall to left costovertebral articulation.
‡ Incomplete turn.
§ 200 c.c. fluid.

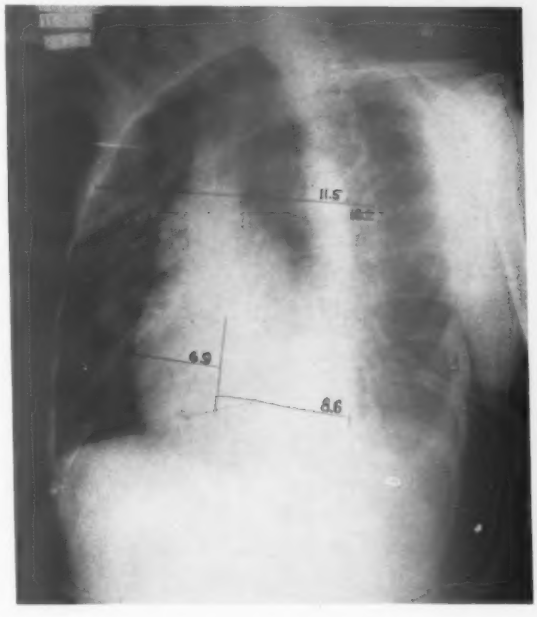
TABLE III

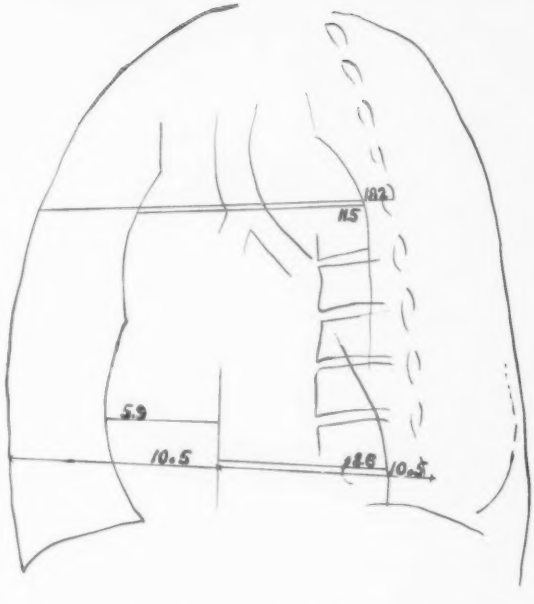
PATHOLOGICAL HEARTS—UNILATERAL ENLARGEMENT

Correlation of the Transverse Diameter of the Heart with the Chest

Case	Age	Index of Rotation	O.T.D.	O.C.S.	O.C.S./O.T.D.	Pathological Findings	
						Heart Size	Heart Weight
			cm.	cm.			grams
H.R.	11		9.8	17.6	1.7	Moderate enlargement	240
J.H.	45	1.8	12.2	21.5	1.8	Moderate enlargement	450
M.J.	43	1.6	9.9	18.5	1.8	Slight enlargement	250
C.H.	60	2.0	13.7	23.5	1.7	Slight enlargement	370
C.M.	57	2.5	12.3	21.0	1.7	Moderate enlargement	460
C.B.	50		15.7	26.2	1.7	Pronounced enlargement	520
E.S.	61	2.3	11.2	20.5	1.8	Slight enlargement	430
G.G.	73	1.6	11.4	21.0	1.8	Slight enlargement	340
Total 8					Av. Index 1.75		



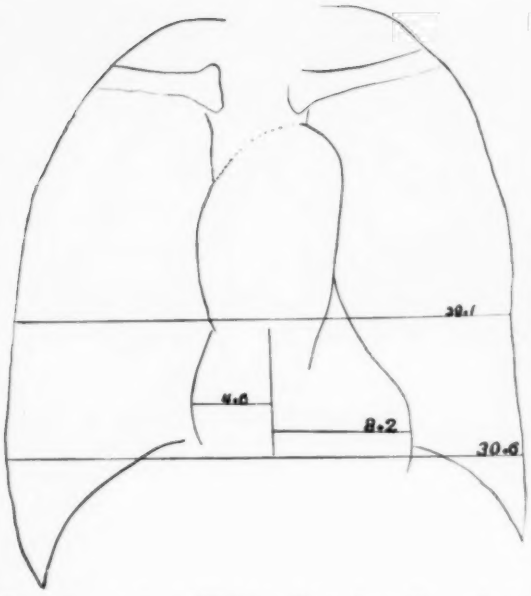


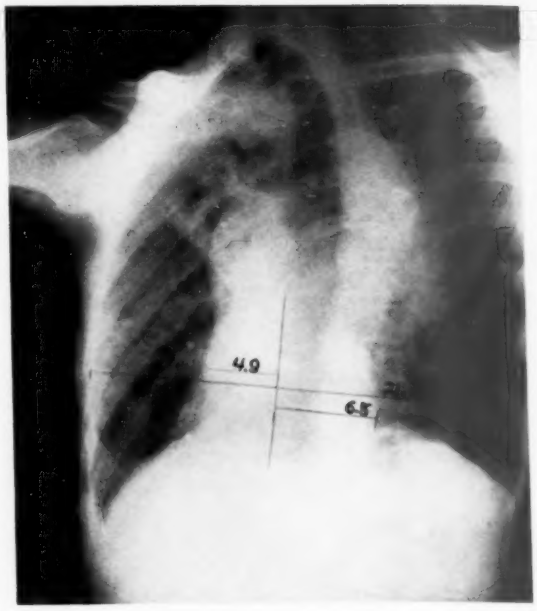


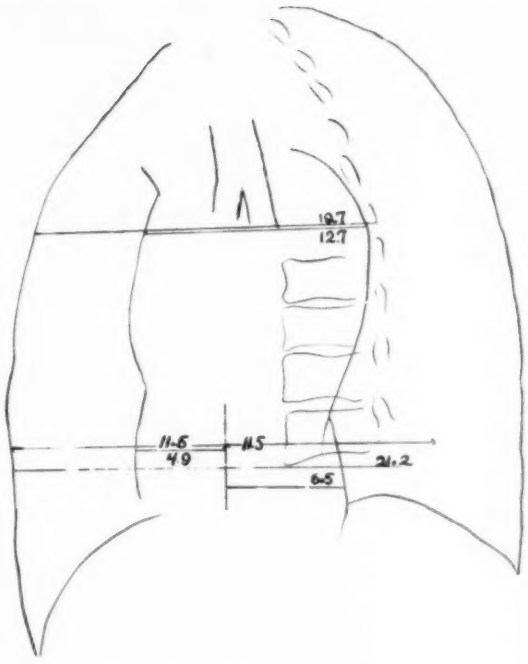
Figs. 5, 6 and 7. Extreme cardiac hypertrophy with enlargement of both the right and left sides. Left oblique film and tracings of a hypertensive individual. Transverse diameter of heart in oblique position 14.5 cm., chest measurement to left costovertebral articulations 21.0 cm., heart-chest index 1.4; weight of heart at autopsy 900 gm., marked enlargement of both right and left sides of the heart, more marked on the left.

nounced hypertension (blood pressure 220/140) during life is illustrated by a left oblique film and tracings in Figures 5, 6, and 7. The main clinical diagnoses were hypertensive heart disease, coronary occlusion, and cerebral thrombosis. The illustrations show extreme cardiac enlargement. The transverse diameter in the oblique view measures 14.5 cm. which is greatly in excess of one-half the chest measurement of 21.0 cm. (index 1.4). At autopsy an enormous heart, weighing 900 grams, and showing enlargement of both the right and left sides, was found. The left ventricle showed more pronounced hypertrophy than the right. The valves were normal except for some stretching due to cardiac dilatation. The pericardium was adherent. Infarcts were present in the myocardium. The figures illustrate the typical appearance of a greatly enlarged heart in the left oblique position with very low heart-chest index of 1.4.

Cases (Table III) which showed enlargement of one side of the heart only were found to have an index between those obtained for normal hearts (av. 2.02) and those whose hearts were found at autopsy to be enlarged on both sides (1.42). The average index for cases of unilateral enlargement is 1.75. There were 3 cases with pure right ventricular enlargement and 5 cases with pure left ventricular enlarge-







Figs. 8, 9 and 10. Slight unilateral cardiac enlargement (left ventricular). The symptoms of this patient (aged seventy-three) related mainly to the gastrointestinal tract. The films show a slight but definite cardiac enlargement. Transverse diameter of heart 11.4 cm.; chest to left costovertebral articulations 21.2 cm.; heart-chest index 1.8. It is apparent that this enlargement affects the left side only (left ventricular diameter 6.5 cm., estimated normal 5.3 cm.). The presence of a slight left ventricular hypertrophy and arteriosclerotic changes was demonstrated at autopsy. Note that the cardio-thoracic ratio is normal in the posteroanterior position. This cardiac enlargement would have been missed if reliance had been placed on the transverse diameter of this single view. The manner in which the position of the interventricular septum is determined and the measurements are made at the aortic arch will be described in a subsequent communication.

ment. In this series of 8 cases, the enlargement at autopsy was described as slight or moderate in all except one case. The heart weights varied from 240 grams in an eleven year old child to 520 grams in a fifty year old adult.

The heart of an elderly individual of seventy-three years is shown in Figures 8, 9, and 10. This case illustrates very well slight unilateral enlargement involving only the left ventricle. The patient was admitted to the hospital for symptoms not relating to the cardiovascular system. These were incidental. He died from a carcinoma of the stomach with metastases to the peritoneum, pleura, and lungs. At autopsy, the only pathology relating to the heart and aorta was a slight left ventricular hypertrophy and arteriosclerotic changes in the aorta. The presence of a slight hypertrophy is suggested by the left oblique film. The

transverse diameter is 11.4 cm. while the chest measurement is 21.2 cm. The former is slightly less than one-half the latter; the index is 1.8. The heart weight at autopsy was 340 grams. Note that a slight cardiac enlargement is readily missed if the measurements of the posteroanterior film are relied upon. The heart comes well within normal limits in this view (normal cardiothoracic ratio obtained from posteroanterior film).

SUMMARY

In summarizing the results concerning this oblique cardiothoracic index, the highest index (2.02) is noted in normal hearts with a range of variations in individual cases of 1.8 to 2.3; the next highest (1.75) was found in cases with unilateral enlargement with common variations of 1.7 to 1.8 in a small series; the lowest index (1.42) was obtained in cases of bilateral cardiac enlargement with a variation range of 1.2 to 1.7. In tabular form they may be listed as follows (Table IV).

Table IV

SUMMARY INDICATING VARIATIONS IN THE HEART-CHEST INDEX IN NORMAL AND ENLARGED HEARTS WITH AVERAGE INDICES FOR THE GROUPS

	Common Variation in Index	Av. Index	No. of Cases
Bilateral enlargement (usually marked)	1.2–1.7	1.42	24
Unilateral enlargement (usually slight or moderate)	1.7–1.8	1.75	8
No enlargement	1.8–2.3	2.02	42

These are listed in this fashion, not because I believe that exactly the same figures would be obtained in another series of cases, but to demonstrate that a definite relationship exists between the size of the heart and this index, large heavy hearts showing a low index, normal hearts a high index, and slightly enlarged hearts an index between these two.

CONCLUSIONS

1. A cardiothoracic index has been defined which permits comparison of the size of the heart with that of the thorax in the left oblique chest film.

2. The accuracy of this index in determining cardiac enlargement has been tested in a group of 75 cases in which the cardiac pathology of all the abnormal hearts was checked by autopsy findings.

3. The normal heart was commonly found to have an index above 1.8 with an average index of 2.0 for the entire normal group.

4. The enlarged heart was practically invariably found to have an index of 1.8 or below.

This work has been made possible through the active cooperation of the Department of Pathology.

Thanks are due particularly to Dr. George H. Whipple and Dr. William B. Hawkins in extending to us various records for analysis and summary.

The many helpful suggestions of Dr. William S. McCann and Dr. Stafford L. Warren regarding the manuscript are likewise appreciated.

REFERENCES

1. Bardeen, C. R. Tables for aid in the determination of the relative size of the heart by means of the roentgen-ray. Am. J. Roentgenol., 1917, *4*, 604–610.
2. Bardeen, C. R. Determination of the size of the heart by means of the x-rays. *Am. J. Anat.*, 1918, *23*, 423.
3. Claytor, T. A., and Merrill, W. H. Orthodiagraphy in the study of the heart and great vessels. *Am. J. M. Sc.*, 1909, *138*, 549–562.
4. Eycleshymer, A. C., and Schoemaker, D. M. A Cross-Section Anatomy. D. Appleton & Co., New York, 1911.
5. Eyster, J. A. E. The size of the heart in the normal and in organic heart disease. *Radiology*, 1927, *8*, 300–306.

6. HAMPTON, A. O., and JONES, T. D. A clinical and roentgenological study of the aorta, with special reference to luetic aortitis. AM. J. ROENTGENOL. & RAD. THERAPY, 1930, *23*, 390–395.
7. KREUZFUCHS, S. Ein neues Verfahren der Herzmessung. *München. med. Wchnschr.*, 1912, *59*, 1030–1032.
8. O'KANE, G. H., ANDREW, F. D., and WARREN, S. L. A standardization roentgenologic study of the heart and great vessels in the left oblique view. AM. J. ROENTGENOL. & RAD. THERAPY, 1930, *23*, 373–383.
9. VAN ZWALUWENBURG, J. G., and WARREN, L. F. The diagnostic value of the ortho-diagram in heart disease. *Arch. Int. Med.*, 1911, *7*, 137–152.
10. VAQUEZ, H., and BORDET, E. The Heart and the Aorta. Translated by James A. Honeij and J. Macy. Yale University Press, New Haven, 1920.

Vol. XXVII, No. 2

TRACTION DIVERTICULUM OF THE ESOPHAGUS*

TEN CASES DIAGNOSED BY ROENTGEN MEANS

By MILLS STURTEVANT, M.D., LOUIS L. SHAPIRO, M.D., *and* ROBERT P. WALLACE, M.D.
NEW YORK CITY

THE following paper will present 10 cases of traction diverticulum of the esophagus. Its purpose is to call attention to traction diverticulum as an entity, particularly to its complications, and to suggest the possibility of its more frequent diagnosis by roentgen means.

Diverticula of the esophagus have been variously grouped. The original classification published by Zenker[17] in 1876 was the simplest, and divided diverticula into two varieties: pulsion, occurring at the pharyngoesophageal junction, and traction, taking their site lower down. Since then knowledge of esophageal diverticula has been increased by pathological study, by roentgen examination and, more and more of late years, by direct observation with the esophagoscope, until in 1926 a published classification[9] listed nine varieties.

This paper will deal with the classical traction diverticulum described by Rokitanski[14] in 1840, as due to a pulling out of the esophageal wall by the adhesion of an inflamed bronchial lymph node and subsequent connective tissue contraction.

These diverticula are found almost al-

FIG. 1. G. L., male, aged fifty-three, had, over a period of years, been repeatedly admitted to Bellevue and other hospitals for heart disease. In despair of ever getting better he committed suicide by cyanide poisoning. This was a Medical Examiner's case. The lungs showed pneumonia but there was no sign of tuberculosis.

FIG. 2. J. G., male, aged fifty-eight, had had at the age of thirty a vague attack which he called pleurisy. He had had no other illness. He was admitted to the hospital for a six days' illness characterized mainly by vomiting. He did not vomit after entering the hospital and made a rapid recovery. No gastrointestinal pathology was discovered except the diverticulum.

* From the Department of Medicine, The University and Bellevue Hospital Medical College, New York University, and the Third Medical Division of Bellevue Hospital, New York City.

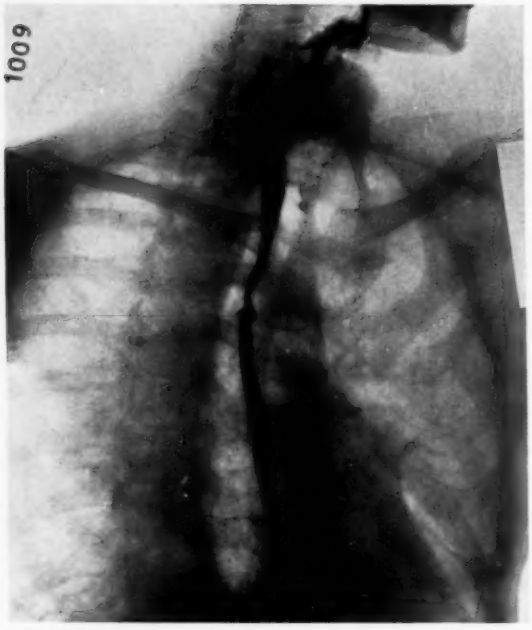


FIG. 3. A. B., male, aged sixty, gave a history of repeated "colds on the chest." He had marked emphysema. This patient complained of dysphagia that came and went. This was of eight weeks' duration.

ways on the anterior or lateral wall where the esophagus comes in contact with the lymph nodes which are to be found about the bifurcation of the trachea. When these glands become tuberculous the process may involve the contiguous esophageal wall. When the abundant resulting connective tissue begins to contract, there is a tent-

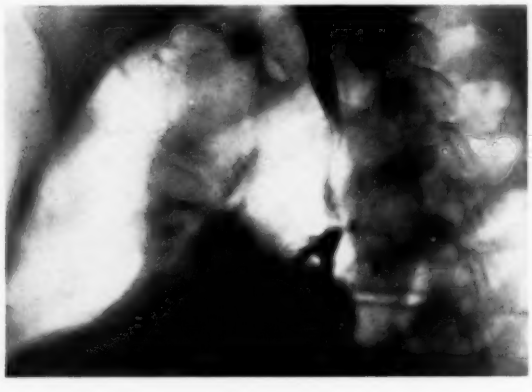


FIG. 4. D. McA., male, aged fifty-five, was admitted to the hospital for cirrhosis of the liver.

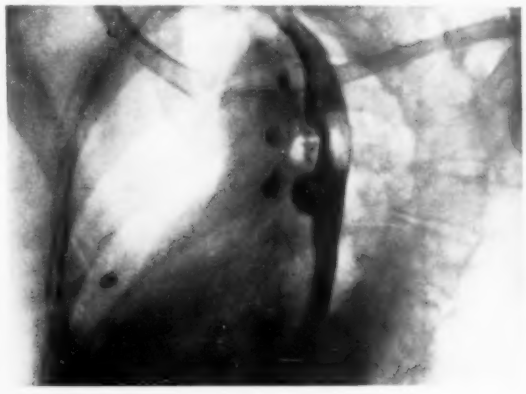


FIG. 5. B. S., female, aged fifty-seven, came to the hospital for catarrhal jaundice. She had a marked curvature of the spine though there was no sign of Pott's disease. She gave a history of empyema at fourteen years of age with operation. The wound drained for two years.

shaped or conical bit of the esophageal wall pulled out. The apex is usually tilted upward. These diverticula are usually single, less often multiple.

By far the great majority of them are tuberculous. Kragh,[11] who has studied 51

FIG. 6. J. W., male, aged sixty-four, complained of dysphagia due to pulsion diverticulum. The traction diverticulum was discovered in routine examination.

cases, says the condition is always tuberculous. Bevermann[2] found 73 per cent tuberculous. Besides tuberculous glands, traction diverticula have been described as due to caries of the spine, mediastinitis other than tuberculous, pleurisy, empyema, pericarditis and cancer. The wall of the esophagus is usually involved in the inflammatory process and rarely is there just an outpulling of the unchanged wall. The circular muscle is thinned out at the tip and overgrown with connective tissue. When this contracts the circular muscle fibers are pulled out through the longitudinal muscle fibers which form pillars at the sides of the diverticulum. The mucous membrane may or may not be involved in the inflammatory process. At the tip is a strand of connective tissue running off in the direction of the axis of the diverticulum, and in this strand are little pockets which contain anthracotic pigment.[5] Pigment is also often found in the wall of the diverticulum all the way to the mucosa. There may be round cell infiltration in the connective tissue strand especially where the lymph node is adherent.

Once formed, these diverticula may enlarge. Food may stick in the sac and irritate it, setting up inflammation. One case has been recorded by Fischer[4] where a wheat kernel with sharp spines was discovered in a diverticulum at necropsy. The inflammation weakens the wall of the diverticulum and under pressure of swallowing it enlarges.

Or there may be perforation. Sternberg[16] has reported 36 instances of the breaking through of the lymph node into the diverticulum. From such a perforation there may be inflammation extending to the mediastinum, pericardium, pleura or lung. The most common complication of this accident is gangrene of the lung, with seropurulent pericarditis and mediastinitis next in order of frequency. In a series of 10 cases of gangrene of the lung studied by Geipel,[6] 4 were due to perforation of esophageal diverticula.

The irritation incidental to traction diverticula has been suggested as a cause of cancer, and Ritter[13] has described 4 cases of cancer which he found associated with diverticula.

Once detected these diverticula should be watched. To prevent their enlargement, their irritation, inflammation, ulceration and perforation, the patient can be warned as to the advantage of a non-irritating, finely divided diet and encouraged to form the habit of chewing his food to a pulp before swallowing.

Two facts in connection with traction diverticulum are emphasized by students of the esophagus, one, that this condition is fairly common, and second that it is rarely discovered during life.

The frequency has been estimated by Starck[15] at 6 per cent of adult necropsies. He calls attention to the technique of Dittrich's Clinic at Erlangen, where the practice was to remove the lungs, heart and esophagus en masse and then open the esophagus from behind, the esophagus being largely sacrificed in the usual method of thoracic necropsy. Heinen[7] found 27 cases in 1,100 necropsies, about 2.4 per cent. On the other hand, Kragh[11] found 51 cases in 536 necropsies.

The fact that traction diverticulum, which is found in 2.5 to 10 per cent of adult post-mortem examinations, is rarely diagnosed during life, depends on two things: first, that usually these diverticula give no symptoms, second, that most of them are so shaped and situated that they do not hold a contrast medium well and so are not readily seen by roentgen means. This fact is commented on by Abel[1] in his book on the esophagus. Carman[3] in his book on "Roentgen Diagnosis of Diseases of the Alimentary Canal" dismisses this form of diverticulum by saying that they are usually found at necropsy. He gives no illustration of a case.

For two and a half years, on the Third Medical (New York University) Division of Bellevue Hospital, all patients giving gastrointestinal symptoms have received as part of their study a complete roentgenoscopic and roentgenographic study in the

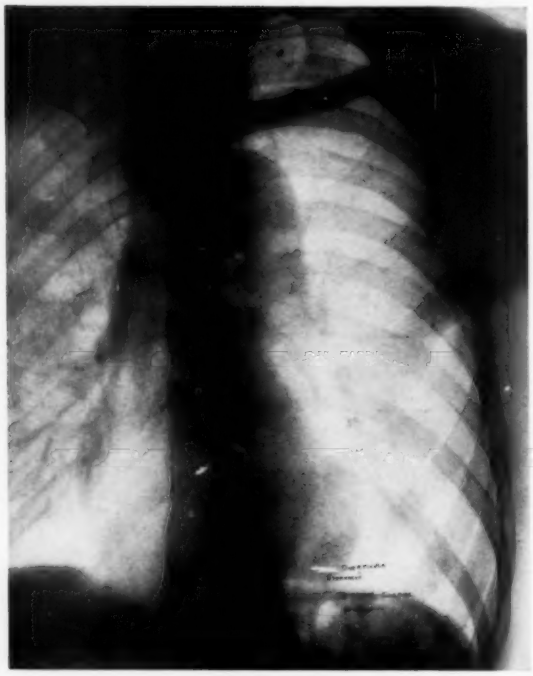


FIG. 7. L. F., male, aged fifty-two, was admitted to Bellevue Hospital for heart disease. The diverticulum was discovered while some dyspeptic symptoms were being investigated. At his death the pathological specimen shown in Figure 8 was obtained.

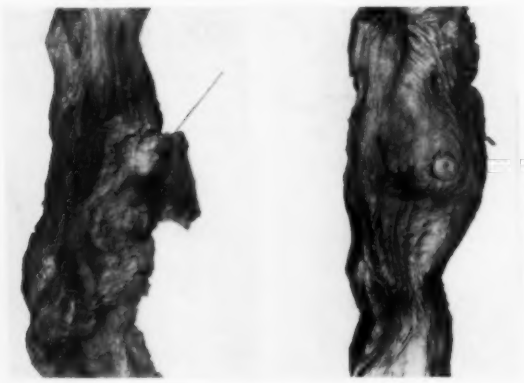


FIG. 8. Pathological specimen of the traction diverticulum whose roentgen study is shown in Figure 7. The left view shows the outside of the esophagus. The diverticulum is filled with cotton. It can be seen how the diverticulum has been pulled out between the longitudinal muscle fibers to point forward and upward. The inside view of the esophagus is given with the diverticulum packed with cotton. There is a small perforation on the apex of the diverticulum, which communicated with a bronchus. This patient died of gangrene of the lung.

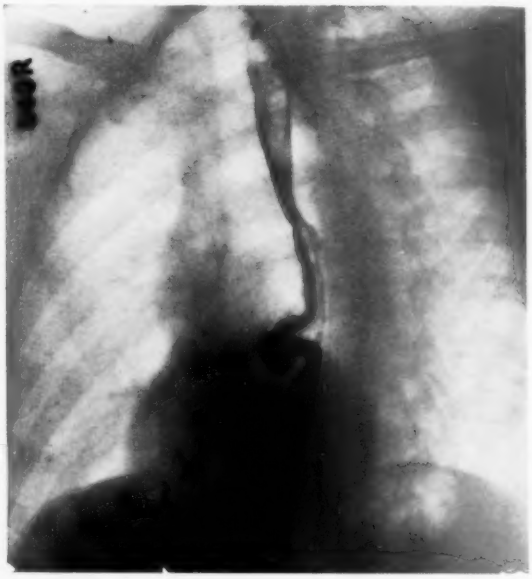


FIG. 9. N. J., male, aged sixty, had had gastroenterostomy three years before. He was a periodic drinker. A short time after the operation while drinking his pain returned and had been with him in attacks ever since. This diverticulum appears to be developing into a traction pulsion type.

FIG. 10. N. G., female, aged fifty, suffered from heart disease. She had influenza and pneumonia in 1917 and "bronchitis" every Winter. She was in congestive heart failure on admission to the hospital. There were no roentgen nor physical signs of tuberculosis.

roentgen department and in addition, a careful roentgenoscopic study by a member of the medical visiting staff. This additional roentgenoscopic practice has been valuable in giving the visiting and house-staff a better coordinated idea of the individual case and has been useful in teaching third and fourth year students.

In this period most of the work has been done by one of us (L.L.S.), who found 5 of the 10 cases which follow. Another of us (R.P.W.), in a shorter service found 3 cases. The remaining 2 cases were found by the roentgen department, one, a patient in the out-patient service, the other a man who for reasons of expediency did not receive ward roentgenoscopy. No unusual techniques are claimed in the discovery of these cases. Some of them have been found with the ordinary barium and buttermilk mixture but all are better visualized and more such diverticula will be detected if the Hirsch[10] esophagus meal is used as a routine measure. This consists of four parts bismuth to one of mucilage of acacia and can be used only if stirred and worked until mixture is sticky. This passes slowly and coats the entire esophagus. The patient should be studied in both the right and left oblique positions, first vertically then prone with the pelvis raised. The latter position has been recommended by Palugyay,[12] and Helm[5] has been able to diagnose a case by this method. The region of the bifurcation of the trachea is to be watched with great care, remembering that no evidence of obstruction will be seen, only a more or less transient disturbance of contour.

There is very little of interest in the clinical data regarding these cases. The diagnoses were varied and of no bearing. One patient had gallstones, one cirrhosis of the liver, 3 had heart disease, one patient had had a gastroenterostomy nine years before for duodenal ulcer. He was alcoholic. Of two females, one had had empyema when ten years old. She came to the hospital for catarrhal jaundice with atonic stomach, loss of weight and asthenia. Another had vomited blood without demonstrable gastric or duodenal pathology. The patient shown in Figure 3 complained of transient dysphagia. The case shown in Figure 6 had also a pulsion diverticulum which gave continuous dysphagia. None of these patients showed objective signs of tuberculosis and none gave a history of tuberculosis, except that one of the women had an adult daughter who lived with her who had pulmonary tuberculosis.

Fig. 11. M. R., male, aged forty-four, was hospitalized for hyperthyroidism. He gave a history of vomiting blood. Repeated roentgen study revealed no evidence of ulcer. This diverticulum gave no symptoms.

One patient was forty-four years old, 6 were in the fifties and 3 in the sixties.

Bevermann's figures for 57 cases were:

11 to 20 years	2
21 to 30 years	6
31 to 40 years	6
41 to 50 years	12
51 to 60 years	13
over 60 years	18

It would seem from these figures that the older the patient, the more likely the diverticulum to form. It is interesting that

no case under ten years of age has been recorded.

To conclude, it can be said in summary, that 10 patients with traction diverticulum of the esophagus are reported, an outline of the pathology of this condition is given, its complications are mentioned and the use of a special contrast meal is recommended for routine use in examination of the esophagus.

REFERENCES

1. ABEL, A. L. Oesophageal Obstruction. Oxford University Press, London, 1929.
2. BEVERMANN, C. Ein Beitrag zur Lehre über Traktionsdivertikel der Speiseröhre. Erlangen, 1904.
3. CARMAN, R. D. The Roentgen Diagnosis of Diseases of the Alimentary Canal. Second edition. W. B. Saunders & Co., Philadelphia, 1921, p. 65.
4. FISCHER, B. Ueber Sondierungsverletzungen und Divertikel des Oesophagus. *Deutsches Arch. f. klin. Med.*, 1903, *78*, 141–160.
5. FISCHER, W. Speiseröhre in Verdauungschlauch. In: Henke, F., and Lubarsch, O. Handbuch der speziellen pathologischen Anatomie und Histologie, Springer, Berlin, 1926.
6. GEIPEL. *München. med. Wchnschr.*, 1904, *51*, 1221.
7. HEINEN, W. Ein Beitrag zur Kenntnis der an der Bifurkation der Trachea gelegenen Divertikel des Oesophagus. *Ztschr. f. Path., Festschr . . . J. C. Senckenberg, Wiesb.*, 1907, *1*, 176–186.
8. HELM, F. Seltene Röntgenbilder des Oesophagus. *Wien. klin. Wchnschr.*, 1918, *31*, 665.
9. HILL, W. Pharyngeal and oesophageal diverticula. *Brit. M. J.*, 1926, *2*, 1163–1169.
10. HIRSCH, I. S. The roentgen ray study of the esophagus. *Interstate M. J.*, 1916, *Suppl. Roentg.*, *2*, 42–67.
11. KRAGH, J. Divérticules tuberculeux, dits divérticules de traction, de l'oesophage d'un boeuf. *Compt. rend. Soc. de biol.*, 1921, *85*, 755–757.
12. PALUGYAY, J. Epiphrenal gelegenes Traktionspulsionsdivertikel der Speiseröhre und Spasmus des Killianschen Oesophagusmundes. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1927, *35*, 769–773.
13. RITTER, C. Ein Beitrag zur Lehre von den Oesophagusdivertikeln. *Deutsches Arch. f. klin. Med., Festschr . . . F. A. von Zenker*, 1895, *55*, 173–189.
14. ROKITANSKY. *Oesterr. med. Jahrb.*, 1840, *21*, 222.
15. STARCK, H. Die Divertikel der Speiseröhre, Leipzig, 1900.
16. STERNBERG, C. Ueber die Erweichung bronchialer Lymphdrüsen und ihre Folgen. *Verhandl. d. deutsch. path. Gesellsch*, 1905, Jena, 1906, 309–311.
17. ZENKER, F., and v. ZIEMSSEN, H. Krankheiten des Oesophagus. v. Ziemssen's Handbuch der speziellen Pathologie und Therapie. Leipzig, 1877, vii.

Vol. XXVII, No. 2

THE DIAGNOSTIC VALUE OF PREPYLORIC AND PYLORIC ROENTGEN FINDINGS*

By ROBERT S. STONE, M.D., *and* HOWARD E. RUGGLES, M.D.
University of California Medical School, Department of Roentgenology
SAN FRANCISCO, CALIFORNIA

THE pylorus has been intensively studied by anatomists and physiologists for many years. Ever since the earliest demonstration of it by roentgen rays, using the gas distention or opaque meal methods, roentgenologists have been adding their contribution to the knowledge of the anatomy, physiology and pathology of the region. In spite of this, it is hard to find anywhere a comprehensive study of the pylorus and its deformities of such a nature that the individual roentgenologist can go to it with his own puzzling case and see the possibilities. It is the aim of this presentation to group abnormal findings to see what causes them, instead of the more usual method of grouping the diseases and describing the deformities resulting from each.

A correct interpretation of the roentgen findings must be based on a knowledge of the anatomical, physiological and pathological conditions that may be present. Anatomically the walls of the pyloric antrum consist of a serous peritoneal outer covering, an outer longitudinal muscle layer, an inner circular muscle layer, a submucous layer, in which is embedded the muscularis mucosae, and the mucous membrane. At the pylorus the circular muscle layer is thickened, forming the sphincter of the pylorus, and the mucous membrane forms a fold over this known as the pyloric valve. The passage through the valve is known as the pyloric canal. As seen on the operating table or after death the pyloric canal is open, but as shown by the roentgen ray it is normally closed. This canal varies considerably in length but as usually seen on roentgenograms it is about 0.5 cm. long and varies in diameter up to 7 mm. A cross-section of the canal may be round or oval or semicircular. When oval, the long axis is in the anteroposterior direction and the two ends narrow. The canal normally passes from the center of a smooth convex end of the stomach to the middle of a flat or slightly concave proximal end of the duodenum.

Physiologically, the control of the opening and closing of the pylorus is still a matter of debate. It is said that normally the pyloric canal opens at the approach of each peristaltic wave, regardless of the acidity of the stomach or duodenum, just as a wave of relaxation precedes a wave of contraction in all hollow organs.[9,13] In actual observation the pylorus does not open with every wave. This function of the muscle proceeds even if all extrinsic nerves are cut and its counterpart can be seen in excised pieces of muscle free from the nerve plexuses found scattered through the intestinal wall. Over and above this ability to contract by itself, irritation of the vagus has a main effect of stimulating activity in the stomach and pylorus, whereas irritation of the sympathetic causes relaxation of both.

In addition to the muscle of the pyloric sphincter, the muscularis mucosae has a separate and distinct action.[8] Just how much this acts in the pyloric canal is not clear but on both the stomach and duodenal sides it causes marked changes in the size and shape of the mucosal folds entirely independent of the action of the muscle layers proper. These folds, while varying, have a general longitudinal arrangement on the stomach side of the pylorus, and a longitudinal or semicircular course in the duodenum. When in evidence in the canal itself they are longitudinal.

Such are the normal conditions. The abnormal conditions are divided here into

* Read at the Sixtieth Annual Session, California Medical Association, San Francisco, Calif., April 28, 1931.

FIG. 1. Case II. Wide pylorus associated with a duodenal ulcer.

five main types. These may be present singly or in combination. The types here discussed are:

1. Increased diameter and pyloric insufficiency.
2. Decreased diameter and failure to open.
3. Elongated pylorus and immediate prepyloric deformity.
4. Excentric pylorus (without other deformity).
5. Irregularities of the pyloric canal walls.

1. INCREASED DIAMETER AND PYLORIC INSUFFICIENCY

A wide pyloric canal or one that while normal in diameter fails to close properly is usually the result of abnormal relaxation of the sphincter muscle. Either may be due to a spasm of the longitudinal muscle layer but such a spasm is usually in one wall only and so makes the canal excentric as well as dilated. In rare cases it is due to tumor infiltration of a relaxed pylorus. It is seldom found in lesions in the pylorus and is, therefore, due to reflex stimulation of nerves or to a lowering of the gastric gradient.[1] That it is not due to hyperacidity is well proved by its presence in achlorhydria.

In itself this finding is not diagnostic of any lesion but it is a warning signal that some trouble is present. It is found in pernicious anemia, achlorhydria, intestinal obstruction, duodenal ulcer and infiltration with carcinoma or lymphosarcoma. It is sometimes seen in cholecystitis, subacute appendicitis and gastric ulcer, but these conditions usually cause spasm.

The following cases illustrate this abnormality:

Intestinal Obstruction: CASE I. J. L., male, aged thirty-one, had suffered for years with cramp-like pains in the abdomen. He had had previous operations at which areas of narrowing of the bowel had been found and entero-enterostomies had been performed. The present roentgen examination showed a pylorus so wide that it was difficult to tell where the stomach ended and the duodenum began. Barium flowed as freely one way as the other through the region of the pylorus. The duo-

FIG. 2. Case IV. Wide pylorus associated with a gastric ulcer.

denum and small intestines were dilated but showed areas of obstruction. An operation following this examination showed a normal stomach and duodenal bulb except for a few adhesions. The obstructive areas showed lymphosarcomatous infiltration.

Duodenal Ulcer: Case II. S. C., male, suffered from attacks of epigastric pain two to three hours after meals. The pain was usually relieved by food. The clinical diagnosis was duodenal ulcer. The roentgen examination showed a very wide pylorus. The duodenal bulb showed a constant barium fleck and incisures from both sides (Fig. 1). The patient was not operated on but placed on Sippy diet with relief.

Tumor Infiltration: Case III. B., female, aged fifty-nine, had complained of indigestion for a short time. Three years before the present examination she had had a breast removed for carcinoma. The roentgen examination showed a wide gaping pylorus. At autopsy the stomach and duodenum were infiltrated with tumor tissue that looked like lymphosarcoma, but no biopsy was allowed.

Gastric Ulcer: Case IV. J. L. F., female, aged forty-seven, suffered from attacks of epigastric pain one to two hours after meals and lasting about two hours. At first these were relieved by food or alkalies but later nothing gave relief. Patient had had tarry stools and had vomited blood. The gastrointestinal series showed a typical ulcer of the lesser curvature with an incisure opposite. The pylorus was wide but in spite of this there was a 30 per cent six-hour retention (Fig. 2). Operation revealed a large ulcer high on the lesser curvature which had slowly perforated and walled itself off from the peritoneal cavity by adhesions. The pylorus appeared normal. The laboratory diagnosis was chronic inflammation.

Subacute Appendicitis: Case V. A. W., female, aged twenty-five, suffered an acute attack of pain across the lower abdomen which localized to the right lower quadrant after a few hours. She was nauseated but did not vomit. Three days' rest in bed largely relieved her but there was residual right lower quadrant pain and tenderness. The roentgen examination twelve days after the acute attack revealed a wide pylorus and definite tenderness localized to the appendix. At operation a small fibrotic appendix was removed which the pathologist said showed chronic inflammatory changes.

2. DECREASED DIAMETER AND FAILURE TO OPEN

A narrow or an apparently absent pyloric canal is a comparatively frequent finding in any large series of gastrointestinal examinations. The deformity may be due to pathological function or pathological anatomy, or a merging of the two. The abnormal functional conditions are pyloric achalasia and pylorospasm. It is very difficult to distinguish these two and most American roentgenologists group them together under pylorospasm. Achalasia is a failure of the pyloric sphincter to relax on the approach of a peristaltic wave. Pylorospasm is an abnormally persistent contraction of the pyloric sphincter.

Achalasia is due to some reflex mechanism, apparently resulting from any visceral sensory nerve irritation. It is found in gastric ulcer, cholecystitis, duodenal ulcer, subacute or acute appendicitis, or any disturbance near the ileocecal valve, pancreatic disease, urinary colic, uremia, arteriosclerosis of the vessels to the abdominal viscera, tabes dorsalis, hysteria, emotional states, tetany, amyloidosis and poisoning by lead, nicotine and morphine. An example of achalasia from nervousness is the frequent observation that the pylorus fails to relax early in an examination but later commences normal activity.

Pylorospasm is probably due to a more direct irritation of the pyloric muscle. Because of the confusion in the literature and the difficulty of differentiating it from achalasia, it is reported as due to all the causes listed above for achalasia. Hurst,[9] who makes the clearest distinction between the two, says that spasm occurs when inflammation invades the pyloric sphincter. However, Stewart and Barber[15] were able to produce what they called pylorospasm in dogs experimentally by indirect irritation of the duodenum, gall-bladder or appendix, as well as by direct stimulation to the pyloric musculature. Kerley and LeWald[10] describe the typical findings of pylorospasm as follows: "On administration of an opaque meal the pyloric end of

the stomach fails to fill; after several minutes this region fills out, but nothing passes through the pylorus. (We refer to the unpalpated stomach, for under forcible palpation in front of the fluoroscopic screen some food may be pressed through the pylorus). . . . No food will be observed passing through the pylorus until perhaps after from 45 minutes to 1 hour. From this time on the pylorus may function in a fairly regular manner, so that at the end of the average emptying time only a slight retention may be present. In other cases the pyloric aperture becomes spasmodically closed and does not relax again for another interval of a quarter of an hour. In this type of case there will usually be a very large gastric retention." It is evident that Le-Wald's spasm is Hurst's achalasia. Köhler[11] says, "If no pyloric lumen can be seen for a considerable time, while there was previously a free passage from the pars pylorica into the first part of the duodenum, that indicates pylorospasm. Frequently the pars pylorica of the stomach appears dilated and hyper-peristalsis is present."

Anatomically a narrowing or inability to open may be due to infiltration of any or all of the layers of the wall with tumor or inflammatory tissue, to fibrosis of the walls with contraction, to peripyloric adhesions or to hypertrophy, with or without fibrosis, of the sphincter muscle. Abnormal thickening of the mucosal folds may be present and show no external evidence, either visual or tactile. The specific lesions that may cause these changes are early carcinoma of the pylorus, pyloritis, pyloric ulcer, healed ulcer, adhesions from a neighboring inflammation and hypertrophic pyloric stenosis of adults. Hypertrophic pyloric stenosis of children also comes in this group but is not discussed.

Pyloritis without ulceration is apparently very rare. Bastianelli[3] described a case of pyloric stenosis in which pathological examination showed inflammatory tissue in the wall as the only lesion. Pyloric ulcers usually produce some other deformity as well as stenosis.

There is a definite hypertrophic pyloric stenosis of adults.[2,3,6,14] There seem to be two possible causes. In some few cases there is a definite history extending back to childhood, proving a congenital origin—or at least the same origin as in congenital hypertrophic pyloric stenosis. Crohn[7] reports an excellent example. The commoner cause is apparently a long-persisting pylorospasm in which the pyloric sphincter muscle becomes hypertrophied and sometimes fibrosed. In some cases of gastric ulcer, cholecystitis or appendicitis that show no improvement in the gastric symptoms after operation, the cause is to be sought in a hypertrophied pylorus which has resulted from a long-continued reflex pylorospasm. These cases frequently show a combination of the defect now under discussion, narrowing of the pyloric canal, with that next to be described, elongation of the pyloric canal.

The roentgen finding in all of these cases is a narrow or absent pyloric canal. The functional conditions can usually be differentiated from the anatomical by repeated examinations or by antispasmodics. They are seldom the same on two different occasions, or for that matter at different times of the same day. At the time of the first examination amyl nitrite or peppermint water may relax a spasm or relieve an achalasia. If the examination can be repeated it is best to give belladonna or atropine until the throat is dry. Achalasia can be distinguished from pylorospasm by palpation under the roentgenoscope. Barium can be pressed through the pylorus if achalasia is present. It cannot be pressed through a true spastic pylorus.

If the lesion is an anatomic one and there is no other deformity than the stenosis, it is impossible to tell the cause of the stenosis. If the stenosis is so marked as to be definitely obstructive, the following points are helpful but not diagnostic. In ulcer cases the stomach is grossly dilated, atonic and lies obliquely across the abdomen with the pylorus to the right of the midline. In carcinoma the stomach is not grossly di-

lated but is frequently contracted so that the pylorus lies to the left of the midline and it does not appear atonic.

The following cases illustrate this lesion:

Pylorospasm: Case VI. C. C., male, aged sixty, had had attacks of epigastric pain fifteen years before that lasted for three years. For the last three or four years he had had epigastric pain partially relieved by diet, to which he would not adhere. He had vomited considerably, usually about three hours after meals. Some blood was seen in the vomitus. The report of the gastrointestinal series was in part as follows: "There is a large out-pouching from the lesser curvature, about one inch in diameter and three-quarters of an inch deep, just above the incisura angularis. Peristalsis passed along the greater curvature but not the lesser. At no time was the pylorus seen nor was the duodenal cap ever filled out. There was a 90 per cent 6 hour retention and a 50 per cent 24 hour" (Fig. 3). The conclusion was, a gastric ulcer, possibly malignant, with reflex pyloric obstruction. Operation revealed a large callous ulcer with inflammatory reaction in the wall extending down to the pylorus.

Fig. 3. Case VI. Failure of pylorus to open due to pylorospasm associated with a gastric ulcer and inflammatory infiltration of the pylorus.

Fig. 4. Case VIII. Narrow pylorus due to hypertrophic pyloric stenosis associated with gastric ulcer.

Pylorospasm and Gastrospasm: Case VII. C. S., female, aged sixty, complained of gastric distress starting four years previous to examination and associated with vomiting. The pain would start on the right side of the back and radiate to the right upper quadrant. There was tenderness over the gall-bladder area and over McBurney's point. The gastrointestinal series showed a narrowing of the entire antral region with narrowing of the pylorus. Cholecystography revealed evidence of a gall-bladder filled with stones. At operation a small thick-walled gall-bladder full of stones but with no adhesions was found and a fibrosed appendix. The stomach, pylorus and duodenum were normal.

Hypertrophic Pyloric Stenosis: Case VIII. A. D., male, aged sixty-four, complained of attacks of pain in the epigastrium two hours after eating which had bothered him for twenty-six years. He had had nausea and vomiting on several occasions and several times had had tarry stools and hematemesis. The gastric acidity was 71 free and 97 total after histamine. In January, 1930, a gastrointestinal series was done and showed a large ulcer crater on the lesser curvature in the pars media of the

stomach. The pylorus was narrow and there was a 50 per cent six-hour retention (Fig. 4). The patient was put on ulcer diet, on which he gained weight and felt better for a while. Then a constant dull uncomfortable feeling was noted in the epigastrium. A re-examination three months later showed the ulcer crater to be very much smaller but the narrowing of the pylorus was more marked. There was an 80 per cent six-hour residue. The pyloric narrowing persisted after atropine and was diagnosed as carcinoma. At operation the old ulcer was examined both from the inside and the outside and found to be well healed. No lesion was found at the pylorus. A Fredet-Rammstedt operation was performed with complete relief of the symptoms. One year later a re-examination showed a recurrence of the ulcer and more marked prepyloric narrowing than before.

3. Elongated Pylorus and Immediate Prepyloric Deformity

Elongation of the pyloric canal as seen by roentgenological means is practically always apparent rather than real. The increased distance between the stomach and duodenum is due to involvement of the prepyloric area. The cause of this deformity, as of the previous one, may be a functional derangement or an organic lesion. The abnormal function may be a gastrospasm of either the muscularis propria or the muscularis mucosae. Localized gastrospasm of the prepyloric region may result from any of the causes listed above for pylorospasm. Because it involves an area which does not normally possess a narrow canal, it is more easily detected, but because it does involve an area where cancer is frequently seen, it raises a more serious diagnostic problem.

If the spasm is due to an extra-gastric lesion it can usually be relieved by antispasmodics, and it varies from time to time just as pylorospasm. In the roentgen examination the narrowed area is usually sharply demarcated from the unaffected part of the stomach. The barium shadow is dense right up to the narrowing and there are usually no irregularities. The outline of the defect may, however, be quite ragged and thin. In gastrospasm due to cholecystitis the narrowing is often spigot-shaped, as was pointed out by Carman.[5] It was shown in Case VII above. If the spasm is due to a prepyloric lesion it will not be relieved by antispasmodics, will not vary from day to day and therefore cannot be differentiated from carcinoma if the causative lesion itself is not demonstrated. It is to be remembered that the defect seen on the roentgen film may be due to spasm of the muscle layer or of the muscularis mucosae. If normal folds are seen in the contracted area it is good presumptive evidence in favor of spasm. Normal rugae do not persist in the presence of organic lesions.

The organic causes of elongation of the pylorus and immediate prepyloric deformity are as follows: Hypertrophic pyloric stenosis; inflammatory infiltration and ulcer; adhesions; carcinomatous infiltration; fibrosis (cicatrization); lues.

Hypertrophic pyloric stenosis when advanced shows as an elongation of the pyloric canal as well as a narrowing. It was discussed above.

Inflammatory infiltrations are seldom present without some other deformity than the elongation of the pyloric canal. Without other deformity they cannot by roentgen means alone be distinguished from annular carcinoma.

Carcinoma of the prepyloric region presents the most serious diagnostic problem. It is not always annular but frequently causes an annular deformity. The cause is unknown, but probably infiltration of the deeper layers influences contractions. The diagnostic points of the deformity caused by this lesion are: (1) It is constant from day to day; (2) it is not affected by antispasmodics; (3) the normal part of the stomach shadow suddenly stops with an almost vertical border; (4) the border of the defect next to the stomach fades gradually in density. In addition, there may be reverse peristalsis, early emptying of the stomach in spite of an apparently narrow pylorus and a point of tenderness over the lesion.

Fibrosis, like cancer, produces an un-

changing lesion which is not affected by antispasmodics but the edges are of definite density and slope more gradually into the normal portion of the stomach shadow.

Adhesions cause defects of varying size and extent according to the degree of the process. Frequently bands of decreased density can be demonstrated in the lesion. Sometimes change of position of the patient changes the deformity. They naturally do not change with antispasmodics. At times it is difficult or impossible to differentiate them from defects of carcinoma.

The following cases illustrate the above deformity:

Prepyloric Gastrospasm: Case ix. D., female, had complained of gas, distention and a feeling of fullness after eating. There was some dyscrasia for fats. The roentgen examination showed a long narrow prepyloric region with slight irregularity of the walls but a sloping demarcation from the rest of the stomach, and a carcinoma-like deformity of the splenic flexure. At operation the stomach, pylorus and duodenum were found to be entirely normal and the splenic flexure carcinoma was removed.

Prepyloric Gastrospasm: Case x. K., female, had suffered with vague indigestion symptoms for some time which were attributed to chronic cholecystitis. Repeated roentgen examinations of the stomach showed a very irregular filling defect of the entire antrum and the density of the shadow very unequal (Fig. 5). At operation no lesion of any kind was found in the stomach or duodenum. There was a chronic cholecystitis.

Fig. 5. Case x. Narrowed prepyloric region due to localized gastrospasm associated with chronic cholecystitis.

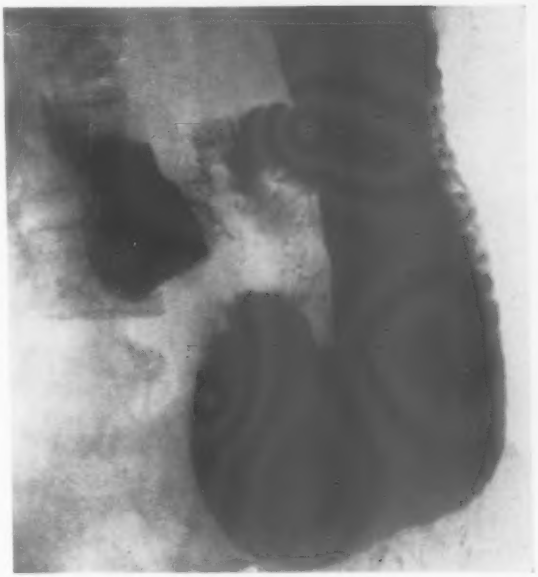


Fig. 6. Case xi. Narrowed pylorus due to hypertrophic pyloric stenosis with no known associated lesion.

Hypertrophic Pyloric Stenosis: Case xi. W. H. H., female, aged forty-six, had complained for years of regurgitation of acid material at night. The amount had been so great that she kept a cup by her bed every night. The symptoms were getting worse. In February, 1931, a roentgen examination of the gastrointestinal tract showed an elongated narrow pylorus with some inconstant irregularity of contour of the adjacent antrum. There was a 90 per cent gastric residue at six hours, and a small residue at twenty-four hours (Fig. 6). An operation on March 7, 1931, revealed an enormously hypertrophied pyloric muscle. There was no evidence of ulceration. There was a small adhesion to the anterior surface of the duodenum but it was not sufficient to cause any constriction. A Fredet division was done. A re-examination on April 15 showed the pylorus still elongated and a 50 per cent six-hour residue but the patient's gastric symptoms were much improved.

Inflammatory Infiltration of the Prepyloric Area: Case xii. M. R., male, aged forty-five, complained of epigastric pain commencing three to four hours after meals. This pain was

Fig. 7. Case xiv. Narrowed prepyloric region due to peripyloric adhesions.

relieved by food or soda. The attacks commenced fourteen years before. He was relieved by Sippy diet and gained weight. The gastrointestinal examination showed a narrowing of the prepyloric region to the caliber of the pyloric canal. The immediately adjacent stomach wall was smooth and sharp. The lesion was found much the same after seven months' treatment, and on each occasion there was a 25 per cent six-hour retention. The patient was sent to surgery because of the persisting roentgen deformity which, while diagnosed as ulcer, did not entirely exclude cancer. The operation revealed a thickened pylorus and prepyloric region. The canal was so narrowed that even the tip of a little finger could not enter it. No ulcer crater was found. The laboratory diagnosis from the resected specimen was nonspecific chronic inflammation.

Prepyloric Ulcer: Case xiii. J. H., male, aged sixty-three, complained of upper abdominal pain two to six hours after eating and at night. The pain was relieved by soda. The attacks started six years previous to examination. Two months prior to examination the patient had a severe attack of almost continuous vomiting with some coffee-ground material and tarry stools. He improved under Sippy regimen. The gastrointestinal examination showed a very long narrow canal in the region of the pylorus. The walls of it were smooth and it was sharply marked off from the stomach. The conclusions from the roentgen examination were: "Obstructive lesion at the pylorus either ulcer or carcinoma but the evidence points more toward ulcer than carcinoma." He refused operation, went home and died some months later of perforation and peritonitis. Dr. Hepplewhite of Chico performed an autopsy and found a large indurated, highly congested mass on the greater curvature of the stomach near the pylorus. The material was sent to Dr. Connor who reported it as a chronic ulcer.

Peripyloric Adhesions: Case xiv. D. McD., male, complained of gas and vomiting for a few months. He was not anemic. No blood was found in the gastric contents or stools on repeated examinations. Three roentgen examinations were performed with an interval of six months between the first and last. On each occasion a contracted prepyloric region was found with irregular walls and no clear demarcation between the abnormal and normal parts of the stomach. At one point there was a band-like constriction across the narrowed part (Fig. 7). A six-hour residue was present at each examination but was greater at the last one than the first. At operation a large mass of omentum was found tucked around the pylorus and antrum, and there were some adhesions. This case resembles very closely a prepyloric carcinoma in its roentgenographic appearance.

Peripyloric Adhesions and Hypertrophic Pyloric Stenosis: Case xv. W. M., male, suddenly felt weak and nauseated while at dinner on July 28, 1926. The next morning he had three dark stools. Occult blood was found in his stools till August 3. On August 7 a gastro-

Fig. 8. Case xvi. Narrowed pylorus and prepyloric region due to an ulcerated prepyloric carcinoma.

intestinal series was negative. He was re-examined four times in October, November and December, showing an increasing deformity consisting of a narrowed very irregular prepyloric region. At operation on January 11, 1927, firm adhesions were found between the pylorus and the under surface of the liver causing a partial rotation of the pylorus. The inside of the stomach was explored and found negative. The pyloric muscle was considerably thickened.

Prepyloric Carcinoma: Case xvi. L. S., male, gave a two months' history of attacks of pain under the lower end of the sternum and a sense of pressure in the epigastrium. He had vomited several times with coffee-ground material in the last specimen. He had lost 10 pounds weight in two weeks. The roentgen examination showed an elongated pylorus and a narrowed prepyloric region. The narrowed portion was markedly irregular and faded into the normal part of the stomach (Fig. 8). At operation an ulcerated prepyloric carcinoma was found.

Prepyloric Carcinoma: Case xvii. E. S., female, aged fifty-five, complained of pain in the epigastrium, distention and belching for two years. The pain bore no relationship to meals. Soda did not relieve the pain. She lost 14 pounds in weight in two months. There was no free acid in the stomach. No blood was found in the stomach. The roentgen examination showed a marked rigidity and narrowing of the prepyloric region. The narrowed portion had irregular walls and there were some small rounded defects extending in to the wide portion (Fig. 9). At operation a large ulcer was found in the prepyloric region which on microscopic examination was found to be a carcinoma.

Fig. 9. Case xvii. Narrowed prepyloric region due to carcinoma.

Fig. 10. Case xviii. Elongated pylorus due to fibrosis of the pyloric and prepyloric regions.

Fibrosis (Cicatrization): Case xviii. S. E., female, aged sixty-six, had complained of epigastric pain between meals for fifteen years. No blood had ever been found in stools or stomach contents. The stomach acidity was normal. The roentgen examination (Fig. 10) revealed a narrow excentric pylorus, a deformed duodenal cap and a large duodenal diverticulum, in December, 1929. Examinations since then show a constantly increasing narrowing but no six-hour retention in spite of this stenosis. The surgeons advised against surgery because of the patient's age but the narrowing was considered to be due to fibrosis.

Luetic Infiltration: Case xix. Female, aged twenty-four, with a family history of lues, positive Wassermann reaction, teeth and other stigmata of congenital lues, complained of stomach trouble. The roentgen examination revealed a long narrow prepyloric channel into which the stomach shadow tapered like a funnel. Under antiluetic therapy this lesion decreased over 50 per cent.

4. EXCENTRIC PYLORUS

The pyloric canal may be displaced from its normal position in the center of the end

FIG. 11. Case XXI. Excentric pylorus associated with cholelithiasis and gastric ulcer.

of the stomach or base of the cap and yet be otherwise normal in its appearance. An oblique view of an oval or semicircular pyloric canal may make it appear to lie excentrically and therefore care must be taken to view the pylorus from all angles. When there is an ulcer on either the stomach or duodenal side of the pylorus it may irritate the longitudinal muscles causing a spasm of these. The result is a pulling of the pyloric canal toward that side. If adhesions form between the gall-bladder and the pylorus they may draw over the pyloric canal. A heaping up of the mucosa on one side due to inflammatory invasion or spasm may make the canal seem excentric. Sometimes for no demonstrable reason the canal is excentric. From the point of view of diagnosis an excentric pylorus is suggestive, therefore, of one of the following conditions: oval pyloric canal, ulcer adjacent to pylorus, adhesions, or inflammation causing contraction of the muscularis mucosae.

Prepyloric Ulcer: CASE XX. B. C., male, aged thirty-one, had complained of mid-epigastric pain one to two hours after meals for three years. He had vomited old food on several occasions and had had tarry stools. He had had some relief from Sippy diet but recently the pain had been almost continuous. The roentgen examination showed a definite irregularity of the prepyloric region on the lesser curvature with the pyloric canal extending in a direct line with the lesser curvature but into the center of the base of the cap. This deformity was the same on a second examination after atropine had been given. At operation a reddened, indurated mass firmly adherent to a rather inflamed and thickened gall-bladder was found on the lesser curvature almost at the pylorus. On palpation an ulcer crater was felt that seemed to have almost perforated the gall-bladder wall.

Cholecystitis and Gastric Ulcer: CASE XXI. J. S., female, aged seventy-seven, complained of a dull intermittent pain in the epigastrium lasting from several hours to all day. It bore no relation to meals. She belched frequently. Thirty years before she had vomited a lot of blood but recovered on bed rest. Six years before a roentgen examination had shown gallstones. At the time of examination her stool contained blood. The stomach acidity was normal. The roentgen examination again revealed gallstones in a gall-bladder that filled and emptied normally. The stomach showed a typical ulcer niche high up on the lesser curvature with an incisure from the greater curvature.

FIG. 12. Case XXII. Excentric pylorus associated with no local lesion but a low intestinal obstruction.

The lesser curvature in the prepyloric region was somewhat flattened but peristaltic waves passed over it. The pyloric canal passed in a direct line with the lesser curvature (Fig. 11). Whether the excentric pylorus is to be regarded as due to gall-bladder adhesions or to spasm of the longitudinal muscles is unsettled in this case as she was not operated upon.

Excentric Pylorus with no Local Lesion: Case xxii. R. W., male, aged sixty-seven, complained of severe abdominal cramps beginning in the left lower quadrant and extending across the abdomen. Induced vomiting or very active catharsis relieved him. Vomiting often brought up food taken some days before. He had had vague indigestion and constipation for one year, but his acute attacks dated back only two months and had come every four to five days. The roentgen examination showed the pyloric canal entering on the extreme left of a duodenal bulb which exhibited a clover-leaf deformity (Fig. 12). It also showed marked distention of the loops of ileum. At operation the stomach, pylorus and duodenum appeared entirely normal but there was a partial obstruction of the ileum from an adenocarcinoma arising in a Meckel's diverticulum. The pyloric and duodenal deformities must have been entirely reflex.

5. Irregularities of the Pyloric Canal Walls

Pyloric canals with distinct angulation of the course of the canal or with markedly irregular walls offer probably the least difficulty in diagnosis of any of the lesions. Carcinomata that start in this region are either annular or by some mechanism cause a uniform annular deformity and do not ulcerate until large. Ulcer in or very near to the pyloric canal is practically the only cause of irregularities in the walls of the pyloric canal. They may cause projection deformities, sharp angulation in the middle of the ring, or convex curvature of the canal. There is usually an associated large gastric retention due to partial obstruction. Many examples of these deformities might be given but two will suffice.

Pyloric Canal Ulcer: Case xxiii. W. G., male, aged thirty, gave a typical ulcer history with finally a partial obstruction. The roentgen examination showed a narrow, angulated canal with a niche (Fig. 13). He was completely relieved by ulcer management.

Fig. 13. Case xxiii. Angulated pyloric canal associated with a pyloric ulcer.

Carcinoma near the Pylorus: Case xxiv. J. D., male, aged forty-three, gave a typical ulcer history extending back for seven years. He had been treated with temporary success with Sippy diet five years ago. For the last two months he had had changed symptoms, now having constant pain and rapid loss of weight. The roentgen examination showed a narrow angulated pyloric canal. In addition the pyloric end of the stomach was very irregular. There was an 80 per cent gastric retention at six hours. The diagnosis of obstructive lesion at the pylorus, probably carcinoma, was made. At operation a tumor mass was felt in the region of the pylorus, about an inch and a half in diameter and attached to the pylorus. It was considered to be an unresectable carcinoma and a posterior gastroenterostomy was performed. If this is a carcinoma it probably arose in or near an old ulcer.

Summary

It has been shown that practically no pyloric or small prepyloric deformity is characteristic of a definite disease or lesion. With few exceptions a diagnosis can be

reached only after careful correlation of all the other roentgenological and clinical findings. Spasms in particular can simulate almost all other lesions and they do not always behave as they theoretically should.

The following deformities and their causative factors are discussed and some illustrative examples cited:

1. Increased Diameter and Pyloric Insufficiency.
   - (a) Achlorhydria.
   - (b) Pernicious anemia.
   - (c) Intestinal obstruction.
   - (d) Duodenal ulcer.
   - (e) Tumor infiltration.
   - (f) Occasionally cholecystitis, subacute appendicitis and gastric ulcer.

2. Decreased Diameter and Failure to Open.
   - A. Functional
     - (a) Achalasia.
     - (b) Pylorospasm.
   - B. Organic
     - (a) Pyloritis.
     - (b) Pyloric ulcers (shallow).
     - (c) Hypertrophic pyloric stenosis.
     - (d) Early carcinoma.
     - (e) Adhesions.

3. Elongated Pylorus and Immediate Prepyloric Deformity.
   - A. Functional
     - (a) Prepyloric gastrospasm.
     - (b) Spasm of muscularis mucosae.
   - B. Organic
     - (a) Hypertrophic pyloric stenosis.
     - (b) Inflammatory infiltration and ulcer.
     - (c) Adhesions.
     - (d) Carcinomatous infiltration.
     - (e) Cicatrization.
     - (f) Lues.

4. Excentric Pylorus (without other deformity).
   - (a) Unusual anatomy.
   - (b) Ulcer adjacent to pylorus.
   - (c) Adhesions, especially gallbladder.
   - (d) Contraction of muscularis mucosae.

5. Irregularities of the Pyloric Canal Walls.
   - (a) Ulcer.
   - (b) Rarely—carcinoma.

Most of the cases were studied at the University of California Hospital. Some of them were examined or operated on at other hospitals. We wish to express our thanks to the surgeons who have called us to the operating room or carefully described their findings to us, and to the internists who supplied us with many of the clinical histories.

REFERENCES

1. ALVAREZ, WALTER C. The Mechanics of the Digestive Tract. Paul B. Hoeber, New York.
2. ARCHER, VINCENT W. Hypertrophic pyloric stenosis in adults; roentgen aspects. AM. J. ROENTGENOL. & RAD. THERAPY, 1930, *23*, 510–515.
3. BASTIANELLI, R. Pylorus spasm and its surgical treatment. *Ann. Surg.*, 1925, *81*, 45–51.
4. BUCKSTEIN, JACOB. Peptic Ulcer. Paul B. Hoeber, New York, 1930.
5. CARMAN, RUSSELL D. The Roentgen Diagnosis of Diseases of the Alimentary Canal. W. B. Saunders Co., Philadelphia, 1921.
6. CHANEY, R. H. Congenital pyloric stenosis in adult life. *J. Med. Ass. Georgia*, 1928, *17*, 57–62.
7. CROHN, B. B. Congenital pyloric stenosis in adult life. *J. Am. M. Ass.*, 1928, *90*, 197–199.
8. FORSSELL, GÖSTA. Studies of the mechanism of movement of the mucous membrane of the digestive tract. AM. J. ROENTGENOL. & RAD. THERAPY, 1923, *10*, 87–104.
9. HURST, A. F. The sphincters of the alimentary canal and their clinical significance. *Brit. M. J.*, 1925, *1*, 145–151.
10. KERLEY, C. G., and LEWALD, L. T. Digestive Disturbances in Infants and Children, Roentgenologically Considered. Paul B. Hoeber, New York, 1923.
11. KÖHLER, ALBAN. Röntgenology. Bailliere, Tindall & Cox, London, 1929.
12. KUNTZ, A. Autonomic Nervous System. Lea & Febiger, Philadelphia, 1929.
13. MCCLURE, C. W., and REYNOLDS, L. Observations on the behavior of the normal pyloric sphincter in man. AM. J. ROENTGENOL., 1921, *8*, 158–162.
14. MAYLARD, A. E. Partial pyloric obstruction. *Brit. M. J.*, 1920, *1*, 626–628.
15. STEWART, G. D., and BARBER, W. H. Gastric hypermotility associated with diseases of gallbladder, duodenum and appendix; a clinical and experimental study. *J. Am. M. Ass.*, 1919, *73*, 1817–1821.

Vol. XXVII, No. 2

ATONIC GALL-BLADDER AND STRAWBERRY GALL-BLADDER*

By PROFESSOR DOCTOR ARMANDO ROSSI

Director of Instruction, The Radiologic Institute of Ospedale Maggiore, the Royal University

PARMA, ITALY

A REPORT by Balli at the Rennione del Gruppo Centro-Meridionale e Siculo (February 3, 1930) which aroused lively interest among the members at the meeting, and an original and complete study by Fichera[1] of the problem of gall-bladder disease (a study from which roentgenologists may derive a great deal of information) have stimulated me to write this article. Roentgenologists as a result of the development of the Graham test are in a position to contribute largely to the solution of the very difficult and interesting problem of the cholecystopathies and to furnish from it new ideas in clinical diagnosis and to face the study of that group of cases which in a broad sense may be classified in the group at the borderline between the normal and the pathologic. And now that a distinguished clinician in perfect collaboration with an equally famous roentgenologist has called our attention to the problem and by using a wealth of cases faced the problem of gall-bladder disease with the intention of clarifying and systematizing this complicated subject, I think it worth while to add the modest contribution of my own experience, referring the results of my observations especially to that form which the authors mentioned have particularly fathomed in their clinical and roentgenologic investigations, and that is the prelithiatic stages (lipoidosis, strawberry gall-bladder) and to draw from it differential ideas, and the relationship of these latter to that special form which was isolated and described clinically for the first time by Chiray, Pavel and Milochevich, atony of the gall-bladder, and which I discussed and illustrated roentgenologically (January, 1927, Societa Medica di Parma).

But before going into the argument proper it seems fitting to recall some facts which have resulted from a long experience with a copious material which has been carefully selected and rigorously controlled; there is much complaint even today by roentgenologists, but particularly by surgeons (as Fichera has observed) that the Graham test gives definite diagnostic information when its result is negative (and that is when the gall-bladder does not fill during the test), but that on the contrary when the result is positive it does not permit one to state that "the gall-bladder is healthy" because surgical control and especially microscopic findings in quite a sufficient number of cases have shown the presence of changes—and at times quite marked ones—in the gall-bladder itself.

Now if we investigate the reasons which have led the roentgenologist to erroneously regard a diseased gall-bladder as healthy we find that many of them depend *on an inaccurate idea of all the elements which must be checked up and evaluated before one can state that a gall-bladder is normal.*

From the beginning of my observations (Rome, October, 1926, Riunione del Gruppo Centro-Meridionale-Siculo) on the Graham test (which I reported at the Relazione del Tanoyja, Trieste, 1925, vi, Congress of Radiology) I have shown the extreme importance of technique in determining the fine details of morphologic changes in the gall-bladder as brought out by tetraiodophenolphthalein, and later in clinical and experimental studies to find out the physiology of the normal gall-bladder (Rossi and Benassi) and in which I found out that it was not sufficient to follow the shadow of the gall-bladder in the different

* Translated from the Italian by E. T. Leddy, M.D., Mayo Clinic, Rochester, Minn.

[1] Fichera, G. Colecistite senza calcolo, lipoidosi cistifellea a fragola e litiasi della vescicola biliare; patogenesi, diagnosi, terapia. *Arch. ital. di chir.*, 1930, *26*, 237–254.

phases of its development, but it is also necessary to follow it accurately and systematically with repeated roentgenographic checks at the time of appearance of the shadow, at the time of variations in the shadow up to the moment of its greater opacity and then at the various stages of its emptying. The most certain method of determining this is to use an "opaque fatty paste" (pasto opaco grasso) and to give it at the time when the gall-bladder has attained its greatest opacity and to prepare the barium with cow's milk as has been advised by Tandoja, Alberti, Abbati, Lapena, and others (it might be mentioned that when this method was proposed the similar but not identical method of Brunner was not known to us) in order to exhaust the cholecystokinetic action on fats and in order to be able to follow at the same time the morphologic and functional changes in the gastrointestinal tract.

Further experience demonstrated to me, which fact has been reported by Busi and others, that the Graham test completes the "indirect syndrome" which information as has been noted, the careful examination of the gastrointestinal tract may furnish us about the biliary tract, while the sum of all these elements in this syndrome maintains the value of the whole.

It results from this that if we wish to find out whether or not a gall-bladder is normal, we must study not only this organ but, since it has intimate anatomical relationships with other organs, the functional relationships between the biliary and the gastrointestinal tracts so that we can draw definite conclusions. Therefore we can state that the gall-bladder is normal when it not only is visible in direct examination and can be seen plainly after tetraiodo but also when its morphologic appearance and its function (completed by observations with fatty paste) its relationship with the gastrointestinal tract and the functional behavior of this latter all appear normal. (Dr. Galli, Thesis for doctorate, R. University of Parma, 1928.)

Following this conception we find that the divergence between the roentgenolgic and clinical findings narrows, and that the information from the roentgen investigation takes on an importance of the first order in the study of gall-bladder disease; if we now analyze accurately the facts on which roentgenologists and surgeons have agreed where the gall-bladder is macroscopically and histologically diseased yet in the roentgenogram appears normal, we find that this opinion was often based either on evidence from the direct examination or on a positive result with the Graham test (without taking into account the finer details: tonality of the shadow, sharpness of outline, and most of all, functionality) or by a study of the function of the gall-bladder but after the injection of substances with a cholecystokinetic effect (hypophysine, atropine, etc.) which may act in a varying way on its function and change its results; but especially after an incomplete study of its function, that is, without making it empty by opaque fatty paste and without taking into account all the modifications in the gall-bladder during its various phases: in short, almost always, especially abroad, there has been omitted an accurate study of the gastrointestinal tract.

If to all this we add that not a few of the things mentioned (technique, importance of the indirect syndrome, etc.) require perfect technique and a special skill we shall understand easily enough how errors of judgment are committed and how the road toward avoiding them can be smoothed out. An important thing I would like to point out is that gall-bladders may have been shown to be morphologically and functionally diseased from a roentgenologic point of view and found to be normal at operation and therefore not removed, and yet the patient finally be driven by exaggeration of his symptoms to another operation and shown to have gall-bladder disease and that the stones present escaped the first surgeon. I would like to summarize some of my experiences with gall-bladder disease without stones.

From 1925 to date I have studied about 1,600 cases of gall-bladder disease roentgenologically. Of these I have been able to follow up about 500 partly clinically but mostly by surgical or autopsy control. I have 32 cases without stones, 22 of these of atony and 10 of strawberry gall-bladder.

I might state at the outset that if this number seems relatively small in comparison with the number of examinations carried out it is due to the fact that cases of lipoidosis and strawberry gall-bladder either were not recognized by the operating surgeon or to the failure to demonstrate stones by the roentgen ray so that the patient was not subjected to surgical intervention but was handled by medical means.

THE NOSOGRAPHIC PICTURE OF ATONY OF THE GALL-BLADDER

In summing up the principal elements which I have collected from a clinical and roentgenologic viewpoint (in which I make use not only of my own experience but also of the illustrious studies which have already been made on the subject and especially the clinical ones), I shall follow the path outlined by Fichera in his monograph because it facilitates a comparison of the various signs of atony with those of lipoidosis and of strawberry gall-bladder.

The loss or attenuation of the contractile power of the walls of the gall-bladder followed by stagnation and concentration of bile and collapse and atrophy of the walls (especially of the tunica muscularis) characterizes atony of the gall-bladder. This condition, known to the anatomists, recognized clinically, was described as a separate entity by Chiray, Pavel and Milochevitch as a result of studies with the duodenal sound. Atony of the gall-bladder is especially to be noted in ptotics, those who follow a sedentary life, the neuropathics, and at times in those with disease of the central nervous system, such as tabes; it seems to affect both sexes equally; it occurs between the ages of twenty and sixty; pregnancy is not a factor; the total duration of the disease is uncertain because it is not uncommon that in a period of years a patient will be sent for study several times with various diagnoses, such as neuropathy, gastropathy, cholecystopathy, etc.

In no case was there fever or elevation of temperature. The main symptoms complained of by the patients were those of biliary dyspepsia and digestive vagotonia; anorexia, sensation of weight and swelling after meals, with dull continuous pain along the costal border; the pain may become worse at times and radiate posteriorly, but generally it is not severe, or regular or periodic; nausea and sometimes vomiting of bile; constipation with attacks of diarrhea at times, and discoloration of the stools which may be soapy or sandy, but which are found chemically to contain much bile pigment.

There is always headache, and it is accompanied by deterioration in the general condition. Objectively we find subicterus, but rarely; in no case is there marked jaundice with noticeable quantities of bile pigment in the urine; the liver is always within normal limits, may be lower than normal and this ptosis is generally associated with general visceroptosis; the spleen is compressed. The gall-bladder is frequently found enlarged and low, and since the abdominal walls are often relaxed and thin it can often be palpated; it is found to be tender but regular and movable; checking up the observation on the same patient, it will be found that the same characteristics are present almost constantly but slight massage will often result in diminution of its volume.

With a duodenal tube abundant, thick, very dark, bile is obtained. The response of the gall-bladder, however, is not constant; at times the introduction of the tube into the duodenum is sufficient, occasionally peptone must be used, or solution of magnesium sulphate in certain cases to produce emptying of the gall-bladder, and at times a strong stimulation by pilocarpine will be needed, otherwise the response will be negative.

The roentgen examination (Rossi, Janu-

ary, 1927, Society of Medicine of Parma) furnishes the following data: by direct examination there is frequently seen the shadow of the gall-bladder which I will describe shortly; we do not see stones visualized by the rays; frequent ptosis of the abdominal viscera especially of the liver, the right kidney and the spleen; when the opaque meal reaches the pyloroduodenal region it is also shown to have dropped; moreover in my cases I have constantly observed a marked decrease in tonus of the stomach and in its peristalsis and even when there is no marked displacement of the pylorus there is to be noted constantly an atonic dilatation of the stomach with delayed emptying even though the contractions of the pyloric region and duodenum may be regular.

With the Graham test carried out intravenously and by the technique I advised we obtain the following data: Morphologically when the gall-bladder following injection is at its maximum visibility (from the eighth to the tenth hour) it is found to be dilated and ptosed; it has the shape of a pear or a banana when the patient is erect; it becomes oval in the prone position; it is lower than the lower border of the liver; its shadow is uniform, and has regular outlines but on comparing its shadow with that of a normal gall-bladder it is paler; moreover, in the erect position the opaque liquid collects at the lower pole of the gall-bladder as a result of which the upper half or two-thirds can be only indistinctly seen in the roentgenogram while in the horizontal position it is completely filled and it can be seen that the region nearest the neck is wider than normal; the walls are flabby, and whereas the normal gall-bladder makes its imprint on the outline of the neighboring viscera, the atonic gall-bladder easily has its outlines deformed (gastrohepaticoduodenal imprint) especially after the opaque fatty meal, when we may observe at times a semilunar shape, or that of a sickle, or a biscuit or the petal of a fleur-de-lis, etc., according to whether the pressure was exerted on one or both the walls of the fundus of the gall-bladder; naturally the characteristics of this deformity can be changed by changing the position of the patient during the examination and by pressure when screening and also by the various stages of fullness or emptiness of the gastrointestinal tract.

More important are the facts obtained by the study of its function; the atonic gall-bladder in general fills late and this is evident in the roentgenograms made after injection of tetraiodophenolphthalein (from six to eight hours), but above all it is slow to empty, and this fact we may determine by observing the patient (kept fasting) from the time of appearance of the shadow of the gall-bladder until it disappears, but it is more advantageous to determine the time of disappearance of the shadow by giving the opaque fatty meal at the time of greatest opacity of the gall-bladder; in this way, as I have mentioned, one has the great advantage of being able to control the relations of the gall-bladder to the pyloroduodenal region and their changes under the stimulus of a fatty substance, and to study at the same time the morphologic changes undergone by the gall-bladder during its period of emptying; in the first case, when we keep the patient fasting we see that the emptying of the gall-bladder takes place after the tenth hour, while during all this time we find gall-bladder shadows slightly differing from each other in position, shape, volume, and tonicity; when on the other hand, we give an opaque fatty meal we get the findings described elsewhere,[1] whereas in the case of the normal gall-bladder we find it has definitely contracted after a few minutes and imprints its outline on the duodenum or pyloric antrum, and by repeating the observations at short intervals (every fifteen minutes) it can be seen that its volume is decreasing steadily and is rapidly fading, to finally disappear; the atonic gall-bladder is observed to take a much greater time to empty.

This may be manifested in various ways.

[1] Rossi and Benassi. *Boll. soc. med. di Parma*, Feb. 25, 1926.

It may be noted that under the stimulus of filling of the duodenum by the opaque fatty meal the gall-bladder which had changed only slightly after the meal suddenly decreases in volume, grows paler and empties from the third to the sixth hour after the meal. Sometimes its emptying is completed after the complete emptying of the stomach. Finally there are cases, rare ones it is true, in which the Graham test is absolutely negative even when repeated after checking up the patient for several days.

If we repeat the roentgen examination after a certain period of medical treatment, prolonged rest, abdominal binders, diets rich in fat, climato-therapy, tonics, electric massage, etc., and when the complaints of the patient have reached a minimum we may find that the Graham test shows that the gall-bladder is returning to normal morphologically but especially functionally.

THE CLINICAL PICTURE OF LIPOIDOSIS AND OF STRAWBERRY GALL-BLADDER

In 1928 one of my assistants, Dr. Galli, in his thesis for the doctorate, described the first cases of strawberry gall-bladder which were observed in my Institute from 1925 to 1927, and described the clinical and roentgenologic pictures. From these observations it may be deduced that the clinical symptoms are those of a chronic cholecystitis and that the roentgen picture presents a mass of data which reminds one of those reported by Balli in 1929 but which differ from them in two respects which I consider important: the constant presence of morphologic and functional changes in the gastrointestinal tract, particularly in the stomach and duodenum, and a marked rapidity of emptying of the gall-bladder after the opaque fatty meal.

Since that time I have been able to assemble other data, which added to those brought out by Fichera and Balli, and Paolucci, assist in throwing light on the interesting and complicated problem of gall-bladder disease without stones.

This affection which we find with great frequency in practice not only in patients sent for study of the biliary tract but also in those for stomach examination, is most frequent in females; it occurs mostly between the ages of thirty and fifty, an earlier age than that for gallstones; it occurs most often in women who have had children but less frequently than do gallstones; chronic infectious diseases (typhoid, pulmonitis, malaria) are frequent forerunners; the onset of symptoms is usually one to three years previous, with an average of about thirteen months; fever may be present, especially of a low grade when the patient comes for examination; pain is a constant symptom; localized under the right costal border it often radiates to the spine, the scapula and to the right shoulder and has exacerbations of a colicky character; the frequency and severity of the attacks are less than in cholelithiasis but increasing severity is reported in almost all cases. Jaundice is often found and sometimes the presence of bile pigments in the urine; this latter is more frequent in the alithic forms than in the calcareous; the hepatic area is seldom found enlarged and it is not often that the gall-bladder can be felt; this may be due to the frequent variations in its volume; hepatic ptosis is common, especially in lipoidosis.

As for the roentgen findings, I think it worth while to discuss those first shown by Balli and which naturally correspond to those reported by Fichera in lipoidosis and strawberry gall-bladder. Balli summarizes as follows the roentgen findings he observed in 7 cases which he studied.

Morphologic Findings: Visibility of the gall-bladder at direct examination. Volume generally increased with relative changes active or passive in neighboring organs; at times decreased visibility, after tetraiodo either by mouth or injection, less than normal. Gall-bladder is pale.

Functional Findings: Filling is generally slow (eight to ten hours after intravenous injection, twelve to fourteen hours after administration by mouth). Emptying almost always delayed. Pain on palpation at roentgenoscopy.

In my own observations in 10 cases I have noticed the following:

At Direct Examination: In about one-third of the cases the gall-bladder was "visible directly" on the roentgenogram and in no case did I see stones; in the majority of cases there was no visceroptosis, while in one-third of the cases the liver and spleen seemed moderately enlarged; with the opaque meal there were found in the gastro-intestinal tract those signs which make up the "indirect syndome" and I think it opportune to insist on the great importance attached to it in these cases; we may summarize the findings associated with it in three groups: (1) disturbances of tone and of gastroduodenal motility, probably from reflex origin in the gall-bladder; (2) deformities of organs in the vicinity of the gall-bladder of varying cause and significance and which have been called the gastro-duodeno-colic imprint, and (3) changes in the position, shape, mobility and contractility of the organs due presumably to the presence of adhesions.

Since the symptoms mentioned may be variable at any given time in a patient it is well to summarize schematically the indirect syndrome which I have found almost constantly in my observations on strawberry gall-bladder, under the following headings: the stomach whatever its position, shape, volume, tonus, shows hypermotility, especially in the pyloric antrum, where often a segmentary spasm of varying duration is noted which reduces the volume of the antrum and accentuates emptying; sometimes we see circumscribed spasm on the lesser curvature of the stomach just as in ulcer, juxtapyloric or duodenal; the pyloroduodenal area is abnormally fixed to the right of the median line and in an elevated position (the stomach therefore appears placed transversely) but at times it is median but retro-displaced; the duodenum shows various changes in its first portion, either it is small, hidden and fills incompletely, or it is normal in size but placed horizontally or lies mesially; often it is displaced backward; it always has an irregular outline and all these deformities persist at subsequent roentgen examination. At times even when maintaining normal volume it is irregular at the apex with narrowing of the superior angle; the second portion much less frequently may be bent over, or inverted, thinned out, or paralyzed; at times the duodenal loop is enlarged, occasionally to almost twice normal size; together with or independent of the deformities mentioned in the bulb or in the second portion of the duodenum or in the greater curvature of the antrum or in the first portion of the transverse colon, we may find typical imprints; according to my experience it is advisable always in these cases to ascertain definitely if they are of biliary origin by excluding all other causes first, and now we have in the Graham test a most valuable method of eliminating all uncertainty. Palpation produces lively pain outside or above the duodenum.

The right colic angle and the first part of the transverse colon may show adhesions to the gall-bladder and one of the commonest findings is an angulation of the transverse colon a few centimeters from the hepatic flexure which makes this segment appear fixed and forms a more or less acute angle easily demonstrated in the erect position. Moreover there is often gas at the hepatic flexure and in the first portion of the transverse colon which tends to remain, and in the proximal colon there is often spasm or tonic contraction of the sphincter of the colon. Another sign pointed out by Busi and which I have frequently noted in cholecystic disease is the presence of segmental dilatation of the first loops of the small intestine.

With the Graham test done as I have pointed out[1] we get the following data:

Morphologically the gall-bladder in one-fourth of the cases is enlarged (usually only moderately), in the remainder it is of normal volume or possibly somewhat smaller; it may be pear-shaped or ovoid, generally hypertonic and deformed; sometimes it is low and hangs below the lower border of

[1] Atti del VI Cong. It. di Radiologia Medica, Trieste, 1925.

the liver but usually it is buried under the lower margin of the liver and does not change its position with the position of the patient; its shadow is usually less dense than normal and is much paler, but in two cases it was perfectly opaque. At times its shadow is uniformly opaque, at times irregularly so, as a result of which it takes on a mottled appearance, with little spots of greater transparency; at times it is spotted with denser, poorly defined areas which make one suspect the presence of stones; the outline is sharp sometimes, at others it is irregular and indistinct; I have found imprints of the stomach, liver, and duodenum in the gall-bladder. Palpation of the gall-bladder produces severe pain and defense spasm of the abdominal wall.

Functionally the gall-bladder is almost always late in filling and becomes visible eight to ten hours after intravenous injection of tetraiodo; at times its filling is very late and cannot be demonstrated until after the opaque fatty meal; the findings in two cases were completely negative. In studying emptying after the opaque fatty meal we find that in the greater part of the cases the gall-bladder changes rapidly in size and shape and in about half the cases the emptying takes place rapidly (thirty to sixty minutes after the administration of the opaque meal the shadow of the gall-bladder fades or returns to its intensity preceding the Graham test provided it was visible at direct examination); at times it is very rapid (and this finding I believe has not been pointed out by others), and corresponds to those cases in which the gall-bladder shadow still visible ten to twelve hours after injection of tetraiodo suddenly appears after the fatty meal and its image may be observed in one or two successive roentgenograms (fifteen to twenty minutes) when it disappears; finally, in one-fourth of the cases the shadow disappears in a greater time than normal (three to four hours after the meal) as if the gall-bladder had attenuated tonicity.

Another observation which I do not think has been previously emphasized is the following: Often after administration of the fatty meal, at the time when the gall-bladder seems well filled in the roentgenogram, the patient complains of recrudescence of his dyspepsia and especially of pain.

From a practical point of view it seems advisable to emphasize how necessary serial roentgenography is, the exposures being made at the shortest possible intervals with the same technical conditions because the gall-bladder usually shows a faint shadow, and since it is so faint unless roentgenograms are made with a rigidly controlled technique, it is easy to miss both filling and emptying so that errors of interpretation will creep in. Are the roentgen findings in these two syndromes sufficiently well explained by the findings obtained clinically, by operation, and histologic examination? I think one can answer in the affirmative.

In *atonic gall-bladder* I have demonstrated in the foregoing that some of the morphologic characteristics of the gall-bladder shown by the roentgen ray are in complete agreement with the anatomical findings in those cases operated on where an atonic gall-bladder could be demonstrated at direct examination; on the other hand, the faint density of the shadow after the Graham test or rather the pale appearance of the gall-bladder and its slowness on filling with the tetraiodo is due to the greater quantity of bile which dilutes the tetraiodo and, secondly, the lessened power of absorption by the atrophied mucosa which is marked in the advanced stages; the particular functional behavior of the gall-bladder, the slowness of its emptying, are to be explained by the loss of tone and by the atrophy, more or less marked, which are found on histologic examination of the walls which can be shown clinically and demonstrated by the different reaction of the gall-bladder to the duodenal sound, which fact Chiray and Pavel consider of prime importance in clinical diagnosis.

Finally, the favorable results which we can obtain by medical treatment by bol-

stering up and stimulating the functional activity of the visceral musculature which can be shown by a return to normal of the roentgen findings confirm the idea that this affection is functional and is accompanied by identical changes in the gastrointestinal tract (gastrointestinal atony).

As for simple lipoidosis and strawberry calcareous gall-bladder, we have here also marked analogy between clinical and roentgenologic criteria as was demonstrated by Balli, Fichera, Ruggeri, Feci, and myself.

When the gall-bladder is visible on direct examination, we find that it has thickened walls, and contains dense bile, at times abundantly; moreover it is my opinion that its visualization is affected by a transparent halo which surrounds it caused by a subserous infiltration by fat which, as Fichera has shown, is found in a certain number of cases (36 per cent).

The functional upsets and the morphologic changes which are constantly noted in this prelithic stage are due partly to reflex phenomena originating in the gall-bladder and partly to perivesicular adhesions which constant in the cases I observed, were present in a high percentage (50 per cent) in lipoidosis and in all the cases of strawberry gall-bladder observed by Fichera, and partly to changes in volume of the gall-bladder associated with an increase of endovesicular pressure and hypertonicity of the gall-bladder walls, or to all these factors variously combined in different cases.

The changes in volume are confirmed by the operative findings, and the faintness of the gall-bladder shadow is therefore to be explained by changes in the mucosa (confirmed by the experimental studies of Giubiani) which in turn change its power of concentration. When the gall-bladder is enlarged there results a dilution of the tetraiodo in the greater quantity of bile which stagnates and thickens; when the volume is normal or reduced, the presence of adhesions hinders the permeability of the gall-bladder. And the non-uniform image, the one which may be called spotted, may be explained by the alveolar structure of the mucosa, described by Fichera in certain cases. In this connection I would like to recall a case reported by Busi at the last Reunione del Gruppo Centro Meridionale Siculo in which the gall-bladder was spotted and which Busi thought was due to stones whereas stones were not present; the opaque bile collecting in greater quantity in the crypts simulated the shadows of stones.

The delayed filling of the gall-bladder is due to the factors already mentioned and which are also the cause of its decreased opacity at cholecystography.

In regard to the time and the modality of emptying of the gall-bladder, it seems fitting to analyze in certain detail the reasons which cause the apparent contradictions in our findings. Balli in the majority of his cases noted that the emptying of the gall-bladder was delayed, whereas, on the contrary, I have observed a rapid or short-lived emptying even though in some of my cases (about one-fourth) the time was greater than normal; in one case the delay was marked while the gall-bladder had a hypertonic appearance and at operation was found to be surrounded by a thick net of adhesions.

Another reason for the difference of behavior of the gall-bladder in simple lipoidosis and in strawberry gall-bladder may be found in the technique employed in the study of function of the gall-bladder opaque to tetraiodo; it is known that the technique of cholecystography, notwithstanding its remarkable development, is not yet standardized and depends largely on the views and personal experience of the roentgenologist who makes the test; in the case in point, for example, it would be sufficient to observe the time of emptying of the gall-bladder by observing the moment of disappearance of the shadow; the patient fasting until the last examination for Fichera to report a case of slow emptying after forty-eight hours, whereas I would base my opinion on the time of emptying provoked by the action of a fat meal to make us give different reports on gall-bladder function.

In the histologic examination we may find an important but not absolute reason: as Balli has shown in his cases, in the walls of the gall-bladder there is found an atrophy of the tunica muscularis, and so it is evident that in these cases the contractile power of the gall-bladder must be less, by which theory we can explain the delayed emptying in the Graham test; but if we consider the findings which Fichera illustrated in all his cases we find that in the prelithic stages the gall-bladder does not always present the atrophy described by Balli especially not the early cases where the tunica muscularis is generally normal, and in the strawberry form it is often shown to be thickened; the findings of Fichera which do not correspond to those of Balli (and not all the cases illustrated by Fichera were studied roentgenologically by Balli) may demonstrate the same thing as my cases, that is, gall-bladders which react normally or more actively than normal may show by their histologic structure the real reason for it, and, on the other hand, will lead to the conclusion that the same result would have been obtained by the two authors if they had studied these cases by the same roentgen examination.

I think that another factor that we must take seriously to explain why in certain cases where in spite of histologic changes we get lively reactions of the gall-bladder is the nervous element. As was shown by Udaondo and Gonalons, Thies, Chiray and Pavel, there is in these cases a hyperexcitability of the vegetative nervous system shown by a tendency toward exacerbations of pain at certain times during digestion and to have these attacks assume a paroxysmal character, to hyperkinesis and spasm of the stomach and duodenum with accelerated emptying of the stomach, to exacerbations of the pain after the administration of the opaque fatty meal and to variations in volume of the gall-bladder demonstrable clinically by various authors and by Fichera himself.

Finally, I think that we must remember that the lesions we are studying may come to us at various stages of their development, and that the studies Balli made were as a whole of early cases whereas I studied only cases referred to me and who presented for the most part well-developed lesions. We may deduce from this that the main cause for such a diversity of findings may be due exclusively to the stage of evolution at which our studies were made; in fact of 7 cases examined by Balli 6 were due to simple lipoidosis and without any sign of adherence to neighboring viscera whereas in my cases the pericholecystitis was constant, and at times there was such an advanced deformity of the gall-bladder that the Graham test was negative and associated with changes in other organs (chronic appendicitis, perityphilitis, membranous pericolitis, duodenal ulcer, etc.).

From the study of my findings I think I can conclude that in the *prelithic stages*, "simple lipoidosis and strawberry gall-bladder" of Fichera *we do not have constant roentgen findings but variable ones according to the stage of development of the disease; and the most probable hypothesis is that which assigns the picture drawn by Balli to the early or least advanced stages of the prelithic form whereas after complete evolution to the advanced stages there will be found the picture which I have drawn and described.*

Having discussed the clinical picture of atony of the gall-bladder and illustrated the various stages of strawberry gall-bladder with lipoidosis, we may summarize and conclude by a study of these two questions: what are the differences between the two forms called alithic cholecystopathy, and do they permit a differentiation between the first group of Fichera and cholecystitis and cholelithiasis? Let us take up the first question.

1. What are the differences between atonic gall-bladder disease and strawberry gall-bladder with lipoidosis?

If we put together the two pictures which I have drawn from my observations we shall see clearly that in the majority of cases both the clinical symptomatology and

the roentgen findings will permit us to differentiate exactly the two forms.

In fact in atony we have the picture of a *purely functional disturbance*, in lipoidosis and strawberry gall-bladder we see more or less well defined the picture of an *organic lesion;* in atony we find that the clinical syndrome is represented essentially by *biliary dyspepsia* with *digestive vagotonia* and *pain* which by its location and radiation calls our attention to the gall-bladder, but it is not very acute, it does not have a periodicity and is not accompanied by fever or jaundice; only exceptionally do we find subicterus and traces of bile pigment in the urine; it is easy to show objectively an enlarged and ptosed gall-bladder in patients with visceroptosis or atrophy and insufficiency of the abdominal muscles, and this picture is constant if we make repeated examinations of the patient.

In strawberry gall-bladder with lipoidosis we find, on the contrary, the *syndrome* of *cholecysitis* or *cholelithiasis*, and at times gastralgia with exacerbation or periodic occurrence of the pain which is more or less frequently of a colicky or ulcer type, and in the history we find that there frequently has been fever; there is icterus, bile pigment is present in the urine; it is not easy to palpate the gall-bladder, probably because of the frequent marked variations in its volume due to the pressure of adhesions which fix it to the under surface of the liver.

If we consider the age and sex of the patient, the presence of chronic disease, the frequency of relapses, etc., we find that while atony is seen equally in young or mature subjects and in men often in the complete absence of any chronic disease and frequently with the onset of symptoms several years previously and with periods of relief, rather than cessation, of symptoms, accompanied by a marked deterioration in general condition of the patient in lipoidosis and strawberry gall-bladder, we find that it involves by preference the female sex; there is often a history of chronic infection; the disease occurs usually between the ages of thirty and fifty and develops rapidly in about a year, usually.

The roentgen examination furnishes a wealth of findings which if correctly coördinated and evaluated are of prime importance in forming a diagnostic opinion; in the direct examination and in that of the alimentary canal we find signs of great importance yet often neglected; with atonic gall-bladder we observe an enteroptosis and what is more interesting a typically atonic stomach; with strawberry gall-bladder with lipoidosis we find no ptosis, but there is present that syndrome of morphologic and functional changes (particularly in the pyloric antrum and duodenum) which characterize the *indirect syndrome of organic gall-bladder disease;* moreover the gall-bladder is almost always visible in atony but in only about a third of the cases of strawberry gall-bladder.

The Graham test, although furnishing data which as a whole are present in atonic gall-bladder, morphologically and functionally gives those findings which we usually get in atony of the viscera, in general, those of *atonic biliary stasis* and on the contrary in strawberry gall-bladder with lipoidosis we get *variable* findings or those of *hypertonic biliary stasis with pericholecystitis* (according to my observations) or of atonic stasis with pericholecystitis (according to Rossi) or without (according to Balli and Fichera).

Now, whereas the atonic gall-bladder is always enlarged and hangs below the lower border of the liver, it is easily found and moved on palpation, has the shape of a pear or banana, its image is pale and uniform, has regular sharp outlines and because of the relaxation or atrophy of its walls may be easily deformed by the pylorico-duodenal or hepatico-renal imprint; on the contrary, in the case of strawberry gall-bladder with lipoidosis the gall-bladder is sometimes enlarged, sometimes of normal volume, sometimes reduced in size so it seldom is below the lower border of the liver, it is usually normal in shape but may be deformed; it is usually pale and more so

than an atonic gall-bladder; at times it may have a spotted or mottled appearance and in some cases may be perfectly opaque; it often has irregular indistinct outlines and makes its own impression on the neighboring organs; finally it is rare that the injection of the gall-bladder shows the presence of a positive or negative shadow of stone and that on palpation it is tender.

Both atonic gall-bladder and strawberry gall-bladder are visualized late (eight to ten hours after injection) but the second in some cases may be seen only after the administration of a fat meal and even then may not be filled (negative findings).

Study of the morphologic and functional behavior of the gall-bladder after administration of a fatty meal (Rossi, Tandoja, Bogden, Brönner) offers much differential assistance; in atony we find that the gall-bladder changes its shape and its tonicity and empties constantly in a time greater than normal (delayed emptying); in the other forms we find either a function similar to that of atony (Balli, Fichera) or a rapid emptying or a very rapid "fleeting" one according to my observations.

Therefore, in atonic gall-bladder we have a unique and well-defined picture; in lipoidosis and strawberry gall-bladder we have variable findings in the second because of the varying stages of evolution of the cholecystopathy and the most probable hypothesis to account for it is that the picture seen here was found in the early forms by Balli whereas mine were obtained in the more advanced stages.

It is evident that when the functional behavior of the gall-bladder is identical to that of the atonic form, the two pictures found by cholecystography may be confused, but if our cases are carefully analyzed either from the facts in the past history of the patient, or from the different morphologic findings in the alimentary canal or from the varying morphologic changes brought out by the Graham test we will find sufficient facts to differentiate them.

The finding of an exacerbation of pain after the opaque fatty meal in cases of strawberry gall-bladder which is absent in the atonic forms is a point to keep in mind; finally an indirect proof is offered by the results of medical treatment; if there results a renewal of changes in nutrition and of visceral tonus in cases with a favorable outcome the chances will be in favor of the atonic form.

Can one of these two forms be supposed to be the early stage of the other? I cannot deny that this may be the case, but up to the present my observations do not support this idea.

What are the roentgenologic findings which permit distinction between the prelithic stage of Fichera and cholecystitis and lithiasis? In answer to this question I may say that at the present state of our observations we cannot make a decision, because even though it is relatively easy to distinguish cholecystitis from a functional disorder (atony) the roentgen signs are many which may be presented both by lipoidosis and by cholecystitis and by strawberry gall-bladder with stones and cholelithiasis. I believe, therefore, that only by making a complete roentgen study of the biliary tract and by being guided in it by the clinical picture which may be drawn from the new conceptions set up by Fichera with a further and larger contribution of observations made by the most intimate collaboration of clinician and roentgenologist will it be possible to come to definite conclusions; at present I think it safer to limit ourselves to a "differential diagnosis of probability alone."

ROENTGENOLOGIC OBSERVATIONS

(Only the more important cases from a roentgenologic standpoint are illustrated in abstract.)

CASE I. *Atony of the Gall-bladder.*

The gall-bladder filled late (sixth hour), is enlarged to about three times normal size; it presents below the lower margin of the liver; it is pyriform, pale, has sharp outlines; its shadow is uniform; at its lower pole it shows a transparent imprint from a haustrum of the colon containing gas (see Fig. 1). At the eighth

Fig. 1. Case 1. Shadow of the gall-bladder six hours after injection of tetraiodo (2 gm.) Merck.

hour it has reached its greatest opacity without well-marked change in its size or volume; the imprint of the colon has disappeared (Fig. 2).

At the tenth hour the same characteristics persist; there is a slight increase in volume and

Fig. 2. Case 1. Eight hours after injection.

Fig. 3. Case 1. Ten hours after injection.

it is lower; the shadow of the colon has reappeared at the lower pole (see Fig. 3).

Ten hours after injection of tetraiodophenolphthalein the opaque fatty meal of Rossi was given; there is seen a slight decrease in volume and opacity of the gall-bladder; the stomach shows signs of atonic dilatation (Fig. 4).

Following the changes undergone by the gall-bladder following the fatty meal it is to be noted that it decreases in volume and empties slowly; even twenty-four hours after injection or fourteen hours after the fat meal it is visible in the roentgenogram while the

Fig. 4. Case 1. After opaque fatty meal.

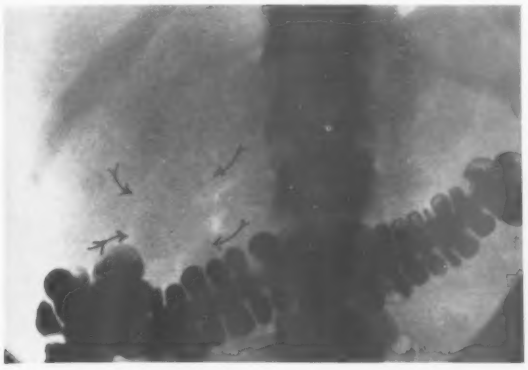


Fig. 5. Case I. Twenty-four hours after injection and fourteen hours after administration of Rossi's paste.

stomach and small intestine are empty and the colon is filled (Fig. 5).

Case II. *Strawberry Gall-bladder* (Vit. N. 20118).

The gall-bladder is visible sixteen hours after 4 grams of tetraiodo (Merck) by mouth; it is of normal volume; slight deformity to kidney shape; it presents below the lower border of the liver; it is pale; invisible at roentgenoscopy (Fig. 6).

After administration of Rossi's opaque fatty meal the gall-bladder is much smaller; it takes on a pyriform shape and is much paler; its shadow is hardly visible in the roentgenogram except external to the first and second portions of the duodenum on which it has made a typical impression, while the bulb of the duodenum is not well shown, retracted, in retroposition and is poorly filled; the second portion is angulated

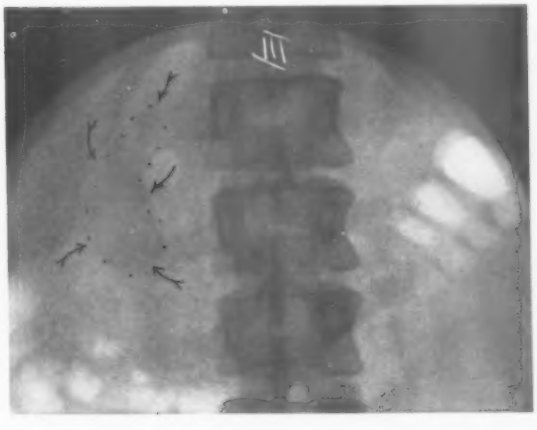


Fig. 6. Case II. Shadow of the gall-bladder fifteen hours after Merck's tetraiodo by mouth.

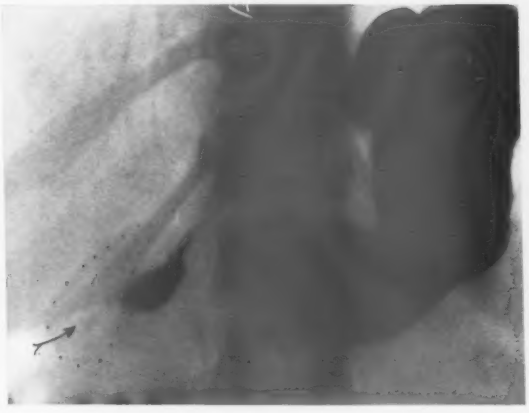


Fig. 7. Case II. Appearance of the gall-bladder, stomach and duodenum after the opaque paste (arrow indicates the crypts).

and lies in the supramesocolic region; the stomach is hypertonic and shows excessive peristaltic activity.

Interesting is the appearance of little rounded shadows of greater density inside the gall-bladder (speckled appearance) (Fig. 7).

Following the shadow of the gall-bladder it is seen that it decreases rapidly in size so that about one hour after the opaque meal it has reduced two-thirds (Fig. 8) and after an hour and a quarter has completely disappeared (rapid emptying).

Interesting in this case is the coincidence of Lane's kink and chronic appendicitis (Fig. 9).

Case III. *Strawberry Gall-bladder* (Rug. N. 32736).

The gall-bladder was late in appearing (15

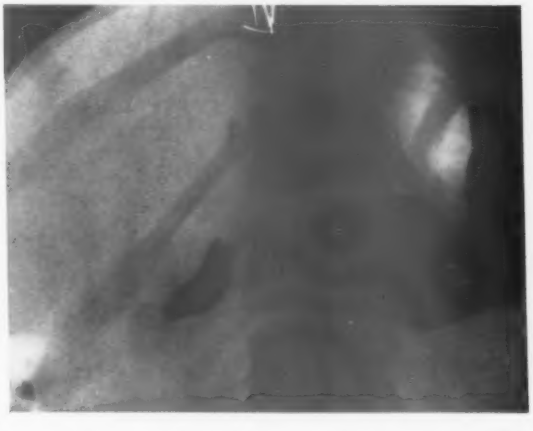


Fig. 8. Case II. About an hour after administration of Rossi's paste.

Fig. 9. Case II. Appearance of the terminal loop of the ileum.

hours after injection of Merck's tetraiodo) only after the administration of opaque fatty meal; it is of normal volume or perhaps a little enlarged, pyriform with its greatest diameter obliquely across the lower margin of the liver by which it is covered almost completely, a little pale, but it could be seen on roentgenoscopy; it was tender on palpation; its shadow is uniform, it makes a marked impression on the duodenum and pyloric antrum; the bulb is

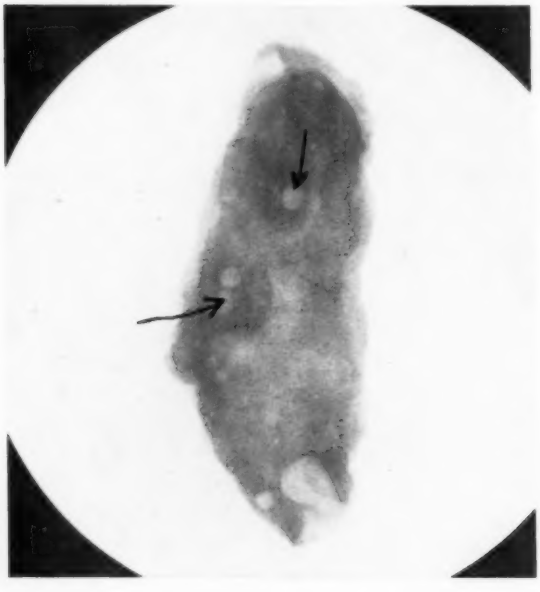


Fig. 10. Case II. Roentgenogram of the gall-bladder; visualization of the crypts.

Fig. 11. Case III. Gall-bladder shadow is visible only after the administration of opaque fatty meal; relationships in the pyloroduodenal region.

retroplaced, and has irregular outlines; the pylorus is drawn to the right and adherent to the lower border of the liver (Fig. 11).

A roentgenogram made fifteen minutes after the opaque fatty meal showed the gall-bladder to be smaller and paler; the duodenal bulb has a lumpy appearance; the second portion is retroplaced; there is hyperkinesis of the antrum with segmentary spasm of the prepyloric region; the right flexure of the colon is distended by gas (Fig. 12). Thirty minutes after the meal the gall-bladder is completely empty (rapid emptying).

It is interesting to note that in this case histologic examination showed hypertrophy of the stratum musculare of the walls.

Fig. 12. Case III. Appearance of the gall-bladder, the pyloroduodenal area and the colon fifteen minutes after the administration of the fat-paste.

Fig. 13. Case III. Twelve hours after opaque meal; relationship of the terminal loop of the ileum reversed into V-shape and of the right colon lying over the first portion of the transverse colon.

By a complete study of the alimentary tract there was demonstrated a bending of the terminal loop of the ileum so that it looked like a V upside down, while the two loops which form the flexure of the right colon were juxtaposed and tightly adherent to each other; operation showed pericolitis on the right (Fig. 13).

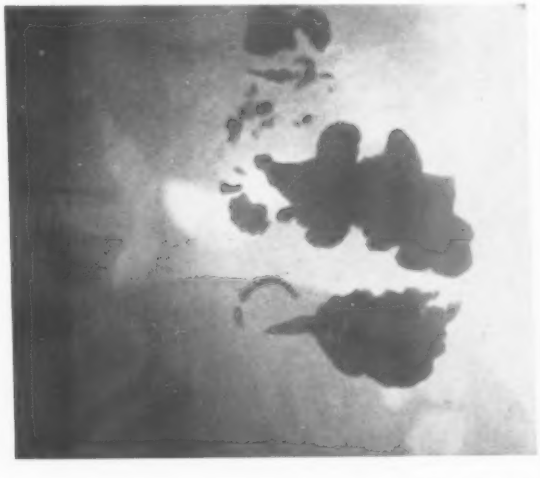


Fig. 14. Case III. Semilateral projection of the right colon "gibbosity" in the anteroposterior direction and retroposition of the cecum and appendix.

Fig. 15. Case IV. Appearance of the gall-bladder twenty-four hours after injection of tetraiodo (Merck).

The roentgenograms in the semilateral position showed a permanent "gibbosity" of the ascending cecum, as a result of which the cecum and appendix were retroposed; gas in the terminal loop of the ileum. No stones in any roentgenogram (Fig. 14).

Case IV. *Strawberry Gall-bladder* (Reb. N. 30347).

The gall-bladder did not appear for twenty-two hours after the injection of tetraiodo (Merck); it is small, elongated, irregular in outline, very pale, paramedian, almost completely covered by the border of the liver, it is low (the lower pole at the level of the transverse process of the fifth lumbar vertebra). The liver is also ptosed (Fig. 15).

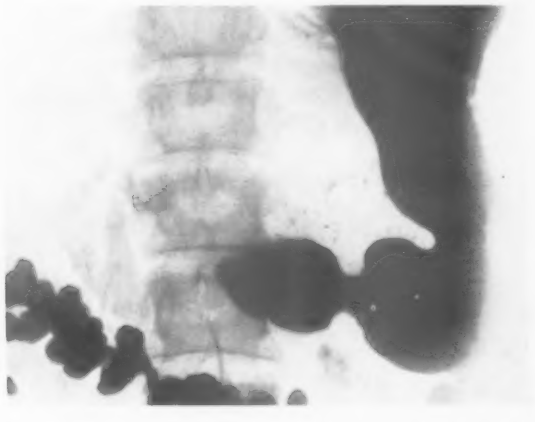


Fig. 16. Case IV. Appearance of the gall-bladder, the pyloroduodenal region and the colon shortly after the fat meal.

After the opaque fatty meal (Rossi) besides the indirect biliary syndrome it was found that the gall-bladder decreased in size rapidly and grew pale while it appeared to be included within the duodenal loop (Fig. 16).

Following the behavior of the gall-bladder at short intervals after the meal it is found that thirty minutes after it the gall-bladder is no longer visible (very rapid emptying); the indirect syndrome is present. No stones seen in any roentgenogram.

Case v. *Strawberry Gall-bladder* (Mar. N. 32581).

The gall-bladder was seen at direct examination; it had an oval shadow, was elongated, pale, enlarged to three times normal size; it was lower than the lower border of the liver with its pole caudad and paramedian (Fig. 17).

Fig. 17. Case v. Direct examination. The gall-bladder is very faint and mottled. Colon full from a previous examination.

The Graham test was completely negative. Study of the alimentary canal showed an "indirect biliary syndrome;" there was deformity and retroposition of the bulb and second portion of the duodenum; duodeno-antral imprint; angulation and medial fixation of the first portion of the transverse colon (see Figs. 17 and 18). No stones seen in any roentgenogram.

Fig. 18. Case v. After the opaque fatty meal; demonstration of the "indirect syndrome."

Case vi. *Strawberry Gall-bladder* (And. N. 20367).

The gall-bladder appeared at the normal time (fourth hour) but it was enlarged, hung below the inferior border of the liver, was pale, had indistinct outlines, but seemed to be oval and paramedian (Fig. 19).

Fig. 19. Case vi. Shadow of the gall-bladder seen four hours after the injection of tetraiodo.

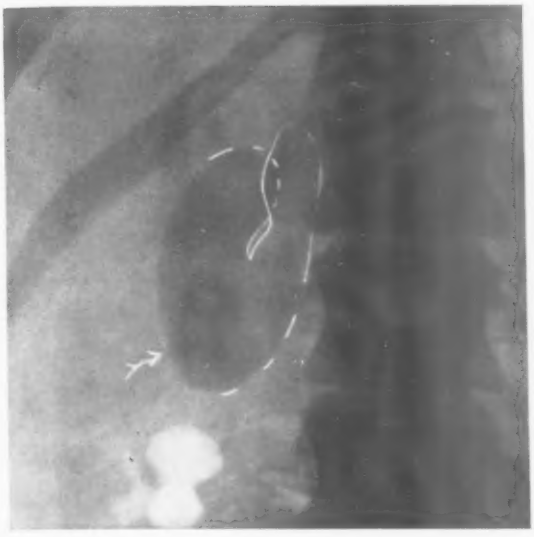


Fig. 20. Case VI. Shadow of the gall-bladder eight hours after injection.

At the eighth hour the gall-bladder was completely opaque; and then it could be seen that it was enlarged and markedly misshapen with the form of a U so that it looked like a fish hook (Figs. 20 and 21).

After giving an opaque fatty meal (Rossi) an indirect biliary syndrome could be seen, then the gall-bladder became smaller and shortly afterward more opaque (Fig. 21), then ten hours after the meal it grew paler and smaller but kept its shape (Fig. 22); about two hours later it emptied completely (Fig. 23).

No stones seen in any roentgenogram; continuing the study of the alimentary tract I found a chronic appendicitis.

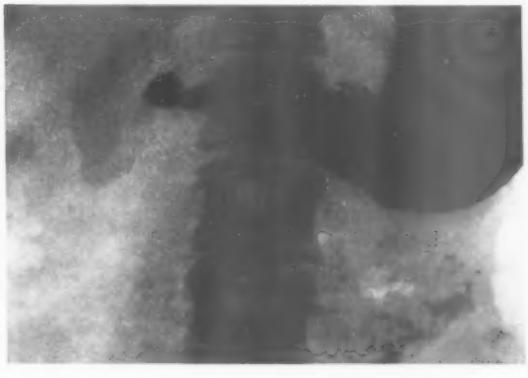


Fig. 21. Case VI. Appearance of the gall-bladder, stomach and duodenum after an opaque fatty meal.

Case VII. *Strawberry Gall-bladder* (Giov. N. 33788).

The gall-bladder shadow appeared late (ten hours after injection), was small, biscuit shaped, perfectly opaque, especially at the lower border of the liver; it could be seen at roentgenoscopy and was very tender to palpation (Figs. 24 and 25).

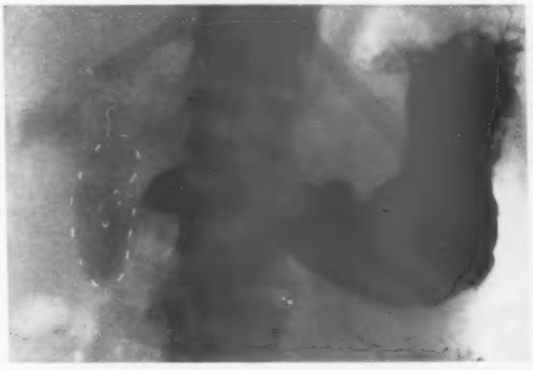


Fig. 22. Case VI. One hour after giving fatty meal. The size and opacity of the gall-bladder are markedly reduced; signs of biliary periduodenitis remain.

thirteenth hour, had sharp regular outline except near the neck, where it appeared unravelled; it was completely covered by the

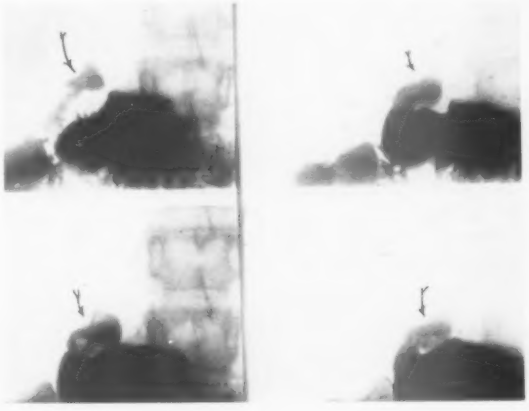


Fig. 23. Case VI. Seriograph of the duodenum two hours after the opaque fatty meal. The gall-bladder is empty; there remains a typical impression on the duodenum.

After the opaque meal (Rossi) the gall-bladder became smaller rapidly and grew pale; the "indirect syndrome" was present; the stomach was large, hypermotile, with segmentary

Fig. 24. Case vii. Appearance of the gall-bladder shadow at the time of its appearance at the tenth hour.

spasm of the antrum, rapid passage of the barium into the duodenum; the bulb was constantly large, but irregularly shaped and retracted; the second portion also lay posteriorly but looked normal; the right colonic angle was adherent to the lower pole of the gall-bladder (Fig. 26).

By repeated examination it was found that the gall-bladder was almost completely empty in thirty minutes.

No stones seen in any roentgenogram. Further examination showed chronic appendicitis.

It is interesting to mention that in this case histologic examination showed hypertrophy

Fig. 25. Case vii. Appearance of the gall-bladder thirteen hours after injection of tetraiodo.

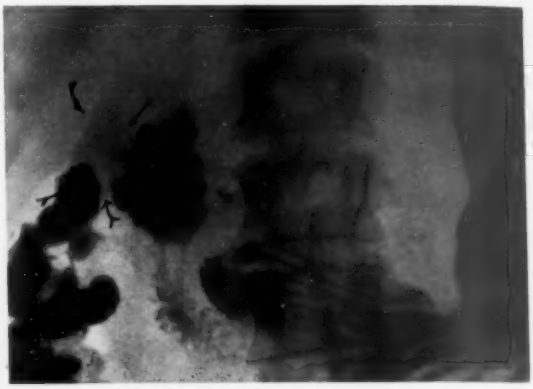


Fig. 26. Case vii. Immediately after opaque fatty meal rapid reduction in size and opacity of the gall-bladder; indirect gastroduodenal signs.

of the tunica muscularis of the gall-bladder (Dr. Docino).

Case viii. *Strawberry Gall-bladder with Stones* (Fa. N. 20642).

Direct roentgen examination showed the functional and morphologic syndrome of duodenal ulcer with tendency to stenosis in the central portion of the bulb, associated with it a concomitant lesion of the gall-bladder was suspected; it appeared in the roentgenogram small, pale, enlarged and deformed; no shadow of stone could be seen in it (Fig. 27).

After the Graham test the gall-bladder was more opaque at the tenth hour after injection of tetraiodo; it was enlarged and hung below the

Fig. 27. Case viii. Direct examination; gall-bladder is visible before injection of tetraiodo; it is pale and misshapen; stenosing duodenal niche at N.

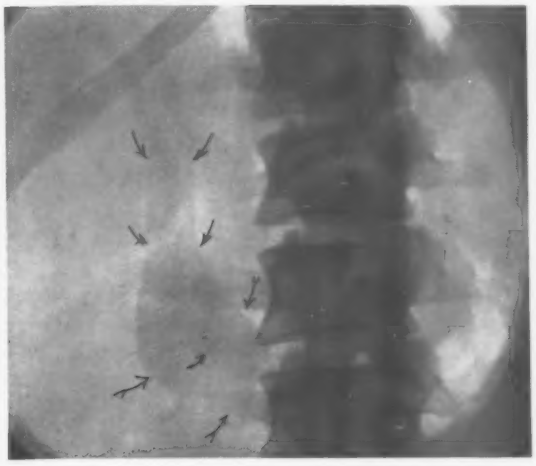


Fig. 28. Case VIII. Ten hours after injection of tetraiodo (Merck) the gall-bladder is more distinct; in it can be seen the shadows of calculi.

lower border of the liver; it had a boot shape and its fundus pointed toward the median line; interesting is the fact that inside its shadow there were six little spots intensely opaque grouped together at the fundus of the gall-bladder (stones opaque to tetraiodo?) (Fig. 28).

On giving an opaque meal (Rossi) the gall-bladder decreased markedly in size while the opacity increased. The shadows in the fundus remained unchanged. There were noted the gastroduodenal changes mentioned above (Fig. 29).

Following the study of the behavior of the gall-bladder under the stimulus of the opaque fatty meal it was noted that it very slowly decreased in size and opacity, and notwithstanding the fact that the stomach was slow in emptying we still find the gall-bladder visible after six hours at which time the stomach was almost completely empty (Figs. 30, 31, 32, 33, 34).

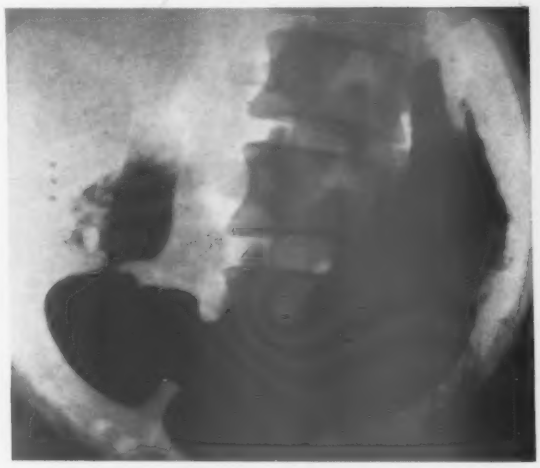


Fig. 30. Case VIII. Forty-five minutes after the opaque fatty meal the gall-bladder is little changed.

The presence of a duodenal niche is seen in Figures 31 and 33 and is marked "N".

It is worth mentioning that this patient had already been operated on for chronic appendicitis and was also suffering from right cystic ovary.

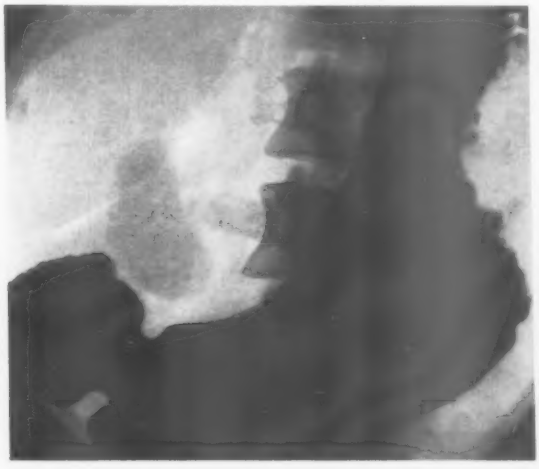


Fig. 29. Case VIII. Appearance of the gall-bladder after the opaque fatty meal; its relationship with the pyloroduodenal region.

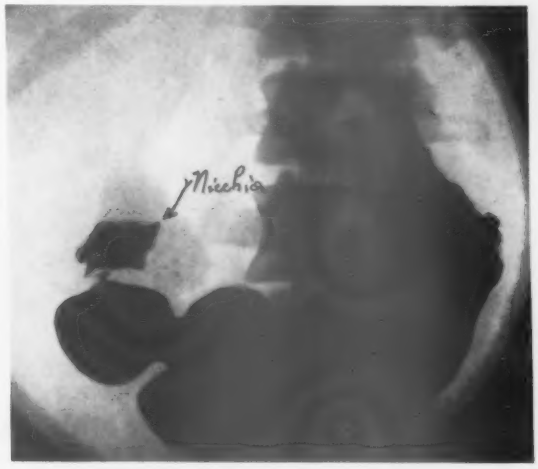


Fig. 31. Case VIII. One hour after the opaque fatty meal the gall-bladder is a little smaller; there can be seen a niche and deformity in the duodenal bulb.

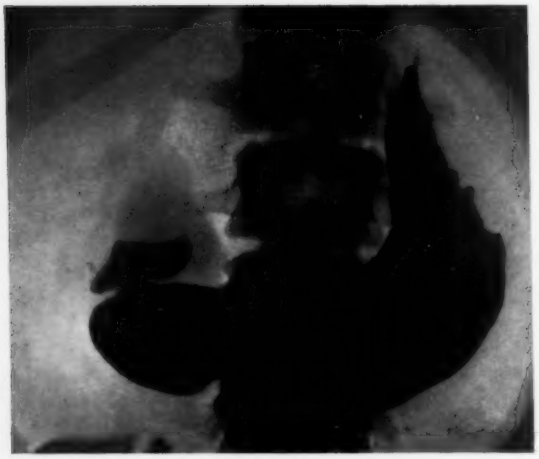


Fig. 32. Case viii. Two hours after; appearance of the gall-bladder hardly changed.

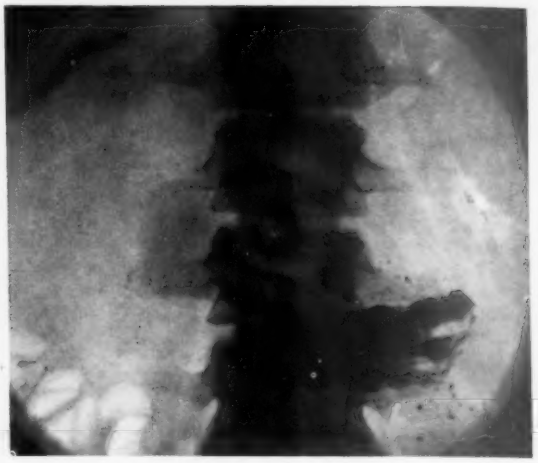


Fig. 34. Case viii. Six hours after the opaque meal. The stomach is almost empty but the gall-bladder is still filled.

Case ix. *Strawberry Gall-bladder with Stone* (Ta. N. 26551).

The gall-bladder was seen fifteen hours after injection of tetraiodo and appeared only after Rossi's opaque meal. It was elongated, deformed at the two ends, it was placed a little obliquely, was completely covered by the hepatic border; it is interesting to note that whereas the superior portion of the gall-bladder was very opaque the inferior part was pale and contained numerous little polygonal areas in a cone (aveolar appearance). The pyloroduodenal region showed the indirect syndrome of biliary periduodenitis (Fig. 35).

A second roentgenogram made fifteen minutes later showed complete disappearance of the gall-bladder shadow and of the calculi.

After following roentgenographically the emptying of the stomach at intervals of about thirty minutes until four hours after administration of the opaque meal, the shadows of the gall-bladder and the calculi did not reappear.

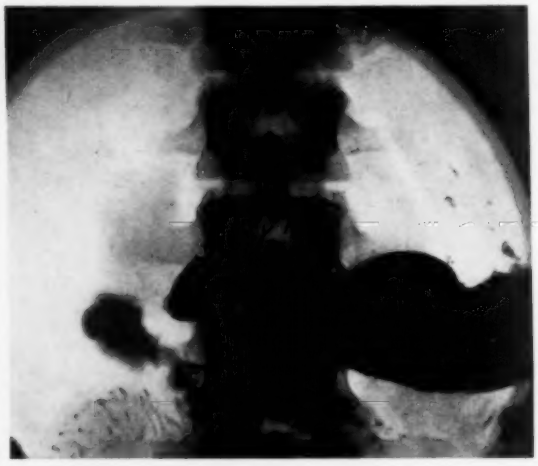


Fig. 33. Case viii. Four hours after. The gall-bladder is smaller and a little paler. Duodenal niche at N.

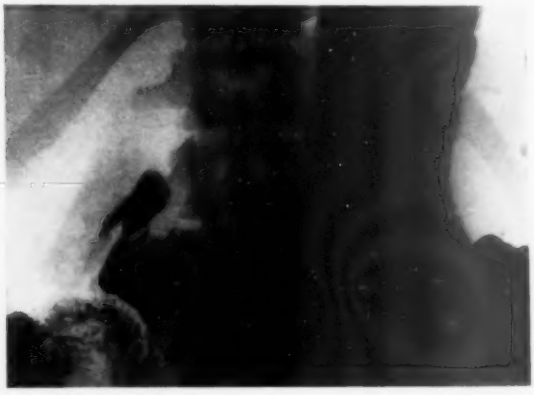


Fig. 35. Case ix. After opaque fatty meal and fifteen hours after injection of tetraiodo (Merck) mottled or alveolar appearance of the gall-bladder.

VOL. XXVII, No. 2

LOCALIZATION OF FOREIGN BODIES IN THE LUNG BY ROENTGEN EXAMINATION*

By HENRY K. PANCOAST, M.D., *and* EUGENE P. PENDERGRASS, M.D.
PHILADELPHIA, PENNSYLVANIA

WITH COMMENTS ON BRONCHOSCOPY UNDER BIPLANE ROENTGENOSCOPIC GUIDANCE†

By GABRIEL TUCKER, M.D.
PHILADELPHIA, PENNSYLVANIA

DETECTION and localization of some opaque foreign bodies in the tracheobronchial tree are attended with great difficulty when the diseased area of lung is of a density almost as great as its foreign body (Figs. 1 and 2). Jackson, Manges, and many others, have contributed a great deal to our knowledge of this subject and in these articles they have analyzed most of the usual and many of the unusual types of foreign bodies and have suggested methods for their localization. We wish to present two cases that have recently come under our observation and to suggest a routine for the preliminary localization and a valuable aid in assisting bronchoscopic removal with biplane roentgenoscopic aid. The principles that are suggested are not new or original with us and they may have

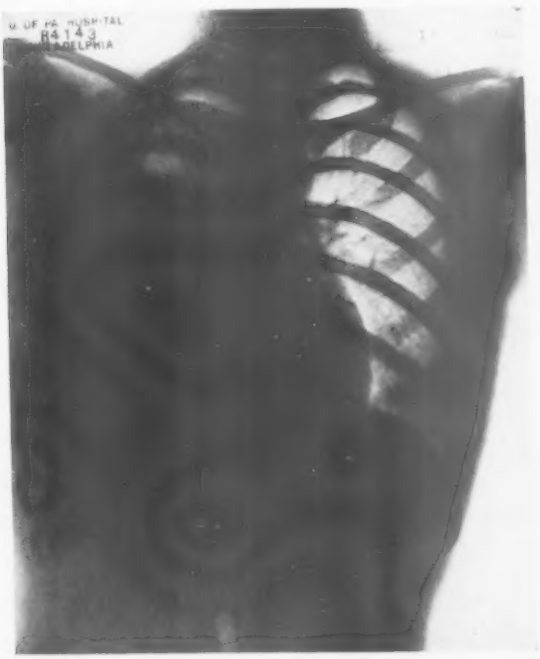


FIG. 1. Case 1. There is a diffuse density of at least the right lower lobe, probably due to a combination of atelectasis and drowned lung. The pleura is probably involved in the process and there is either thickened pleura or a pleural collection. The heart is displaced to the right and there is compensatory aeration of the unaffected lung.

FIG. 2. Case 1. Right lateral view of the same case as Figure 1. The foreign body can be seen at *A*. The right lower lobe is dense. The middle lobe bronchus has had lipiodol introduced into it. *B*. There is some posterior displacement of the heart and compensatory aeration of the right upper lobe.

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pa.
† From the Bronchoscopic Clinic, Hospital of the University of Pennsylvania.

been used as an aid in roentgenoscopic guidance during bronchoscopy many times before, but we have not found any reports in the literature comparable to our experience. The method is simple and has been of invaluable aid to us in two cases, and it is because of our fortunate experience that we have felt justified in presenting this report.

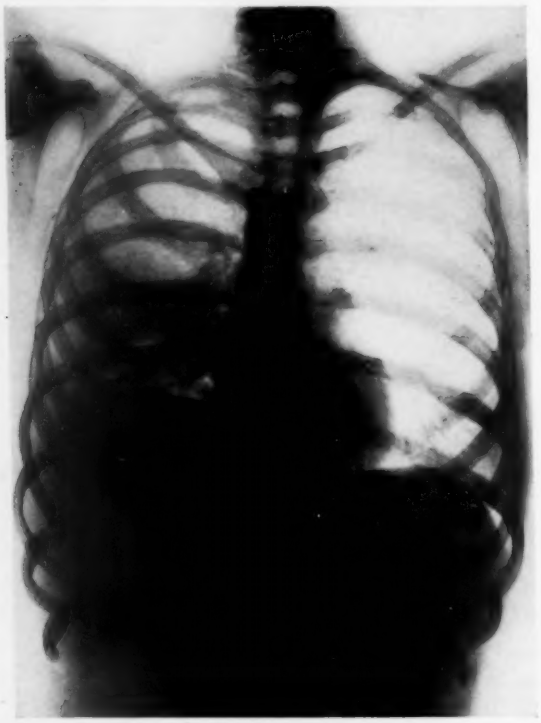


FIG. 3. Case 1. Posteroanterior roentgenogram made elsewhere, prior to present admission. Note the density of the shadow in the right lower chest.

In 1927, one of us[1] reported a combination table that was utilized for reduction of fractures and removal of foreign bodies with the aid of biplane roentgenoscopic guidance. Since that time manufacturers as well as ourselves have made many improvements and modifications of the table, but the essential principles have remained the same, i.e., it is possible to obtain roentgenoscopic observations of a given foreign body in two planes, each plane being at right angles to the other, thereby enabling one to localize a foreign body accurately and assist in guiding the bronchoscopist in his manipulations of the bronchoscope. Our table is so arranged that one oil immersed roentgen unit is underneath the patient and the other unit is on the patient's right side. The roentgenologist makes all of his observations from the patient's left. It must be readily realized that foreign bodies in the right lung will show more distortion than those situated in the left lung, because the former are nearer the source of the energized roentgen tube and farther from the roentgenoscopic screen.

On November 20, 1930, we were requested by Dr. Gabriel Tucker to make a roentgen examination of the chest of a girl, the history of the case being as follows:

FIG. 4. Case 1. Right lateral view showing foreign body at *A*.

CASE 1. A. T., female, aged fifteen, admitted to the service of Dr. Gabriel Tucker, Hospital of the University of Pennsylvania, November 20, 1930.

[1] Pendergrass, E. P. A combination table for bronchoscopic removal of opaque foreign bodies and for reducing fractures with roentgenoscopic guidance. AM. J. ROENTGENOL. & RAD. THERAPY, 1927, *18*, 73–75.

Chief Complaint. Pain in chest, cough with occasional blood-streaked sputum.

Present Illness. Three years ago the patient had a tooth extracted and following this, she developed a wheeze in the right chest. The

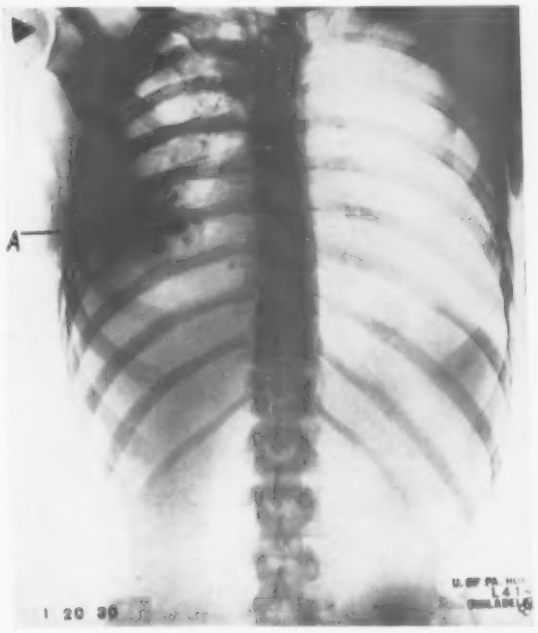


Fig. 5. Case 1. Sagittal view of the chest in the erect posture in the anteroposterior direction. Note that the piece of tooth can be seen easily at *A*.

wheeze disappeared in six months and about six months later a dry cough began. One night she was awakened by a sharp pain in the chest. She was under a doctor's care for five weeks without any improvement. The patient later was referred to a hospital in another city where roentgen examination showed a foreign body (tooth) in the right lung (Figs. 3 and 4). An attempt to remove it was made on five occasions.

Past Medical History. Negative except for aspiration of the foreign body detailed above.

Family History. Negative.

Physical Examination. By Dr. O. H. Perry Pepper.

The patient is a pale, tuberculous looking girl of fifteen. The examination is limited to the thorax.

Inspection. The entire right chest expands less than the left, and the lower portion moves less than the upper.

Palpation. Fremitus is normal over the left chest, absent over the right lower chest, hyperresonant over the right upper chest.

Percussion. The entire right lower and middle lobes are flat, elsewhere there is hyperresonance. The heart is normal in size and displaced slightly toward the right.

Auscultation. Breath sounds are vesicular in type over the left lung and right upper lobe. Over the right lower and possibly the middle lobe, there is tubular breathing.

Conclusion. Foreign body obstructing the right lower bronchus and possibly the middle bronchus. Compensating emphysema right upper lobe. Heart displaced toward the affected side. Pleural thickening right base and extending upward posteriorly.

Blood Wassermann, negative. Blood count, secondary anemia with hemoglobin 62 per cent; white blood cells, 23,000.

The *roentgen examination* of the chest showed a diffuse density of almost the entire right lung (Figs. 1 and 3). In the lateral views (Figs. 2 and 4), it was possible to detect a shadow that was regarded as a foreign body (piece of a tooth).

Fig. 6. Case 1. Right lateral view of chest in the erect posture on the Potter-Bucky diaphragm. The foreign body is seen at *A*. The lipiodol in the middle lobe bronchus is seen at *B*.

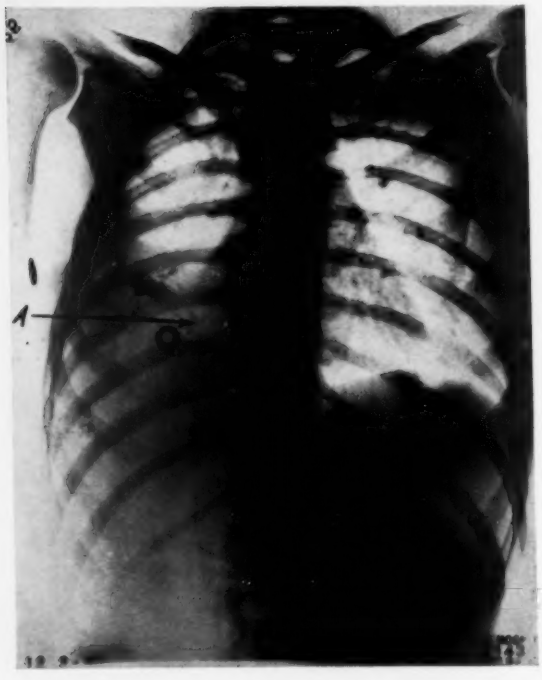


FIG. 7. Case 1. Markers have been placed near the line of the foreign body in two directions. Care was taken not to place them directly over the foreign body, because we did not wish to obscure it. A square piece of lead was used on one side of the body and a round marker was used on the other (and a record of the last location was made) so that the roentgenographic appearance would not cause confusion. *This roentgenogram was made in the anteroposterior direction with the patient lying on the back* and the tube centered over the midline of the body on a line with the markers and the shoulders thrown back in the position for bronchoscopy. Compare this view with Figure 5 which was made in the erect posture.

This foreign body had been demonstrated at the hospital where the patient was previously admitted.

The foreign body could not be seen in either one of these views by the ordinary roentgenoscopic screen. The foreign body could be seen faintly with the Potter-Bucky diaphragm on which a roentgenoscopic screen had been mounted and with the aid of a magnifying glass. We therefore made roentgenograms of the chest using the Potter-Bucky diaphragm (Figs. 5 and 6). By this method it was possible to get rid of the lung density and see the foreign body more clearly. For some time we have been using this method in chest cases other than foreign bodies and have found it extremely valuable as an aid in diagnosis where the density tends to obscure lung detail. (Our reason for this was probably suggested by Dr. Jackson's teachings: "Every obscure lung lesion should be regarded as a foreign body until it is proved to be otherwise.") By this method abscess cavities have been demonstrated when they were obscured in the ordinary roentgenogram by the overlying pleural thickening or collection.

An attempt was then made to localize the foreign body by the bronchoscope with the aid of roentgenoscopic guidance. The attempt was unsuccessful because the foreign body could not be seen, even using the Potter-Bucky diaphragm on which a roentgenoscopic screen was mounted. Roentgenograms were made with the bronchoscope and forceps in position and showed that the proper bronchus had not been explored. Further roentgen studies were made.

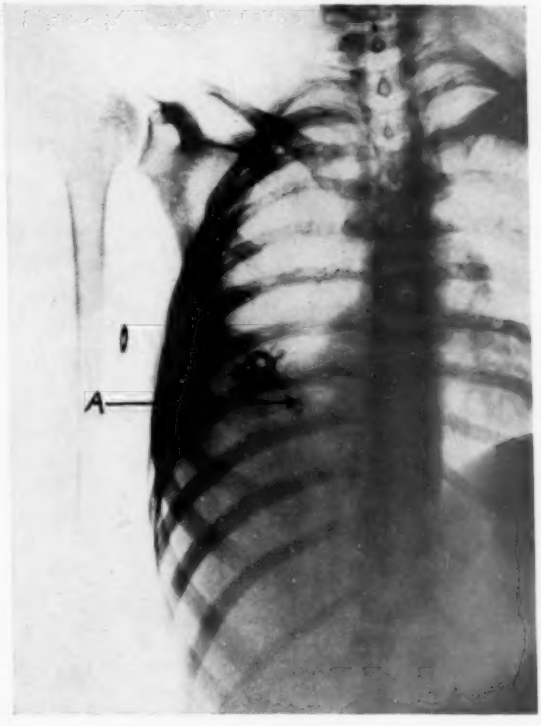


FIG. 8. Case 1. The roentgenogram was made in the anteroposterior position with patient lying down, shoulders thrown back and the tube centered over the markers. Note that the foreign body, *A*, has changed its position relative to the markers. The information obtained in this roentgenogram would approximate more closely that which would be utilized in employing the central ray during roentgenoscopic guidance. Compare the appearance here with that seen in Figure 7.

Fig. 9. Case 1. Left lateral view with patient in the recumbent posture, and shoulders and upper extremities thrown back in position in which the bronchoscopy would be performed. The foreign body can be seen at *A*. It is interesting to compare the appearance seen in this roentgenogram with that illustrated in Figure 6. Note the marked difference in position of the domes of the diaphragm with relation to the foreign body.

At this time, opaque markers for localization of the foreign body were used, making it possible to guide the bronchoscopist by the markers instead of the relatively nonopaque foreign body. The markers were placed and roentgenograms were made (see Fig. 7). We then made an additional study with the patient in the same position (Fig. 8), the only change made being the centering of the tube. The lateral view utilizing the same technique is seen in Figure 9.

The patient was given a transfusion on November 30 because of the secondary anemia and general state of health.

Bronchoscopy for removal was performed on December 3 by Dr. Gabriel Tucker. Considerable pus was found in the tracheobronchial tree. In order to grasp the foreign body it was necessary to dilate the strictured bronchus with stiff spring forward grasping forceps. Then the tooth was grasped under roentgenoscopic guidance and removed in contact with the end of the bronchoscope (see Figs. 10 and 11).

On December 8, the patient was discharged. The patient was expectorating more pus since the removal of the foreign body. She was then sent back to her referring physician for observation and treatment.

Case 11. R. G., male, aged twenty-nine, admitted to the service of Dr. Gabriel Tucker, Hospital of the University of Pennsylvania, December 22, 1930.

Chief Complaint. Attacks of coughing, dry in character, nine years' duration. Hemoptysis during the past month.

Present Illness. About nine years ago the patient had twelve teeth extracted. He began to cough as soon as he came out of the gas anesthesia. He has had the cough since. On November 28, the patient had a hemorrhage from the lung, coughing up approximately one-half cupful of blood. Since that time he has had several hemorrhages. The patient had a roentgen examination of the chest which was negative for any evidence of tuberculosis. The patient was then referred to a hospital in

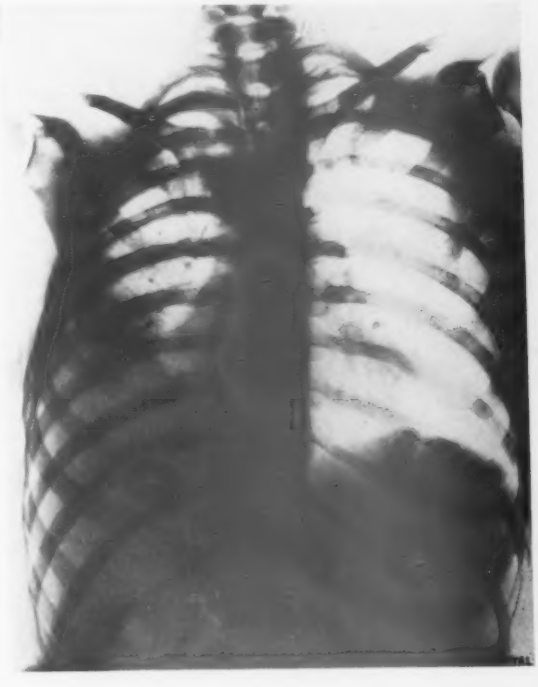


Fig. 10. Case 1. Anteroposterior roentgenogram made the day following the removal of the tooth.

FIG. 11. Case I. Lateral view made after removal of the tooth.

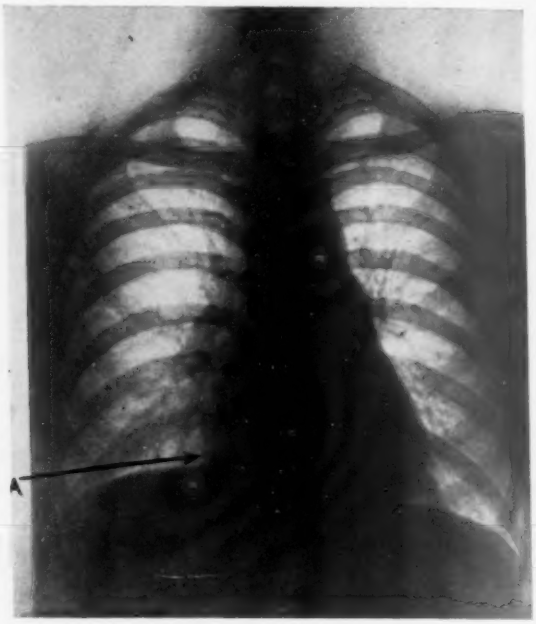


FIG. 12. Case II. Posteroanterior roentgenogram in which it is possible to see a faint shadow of a piece of tooth at *A*.

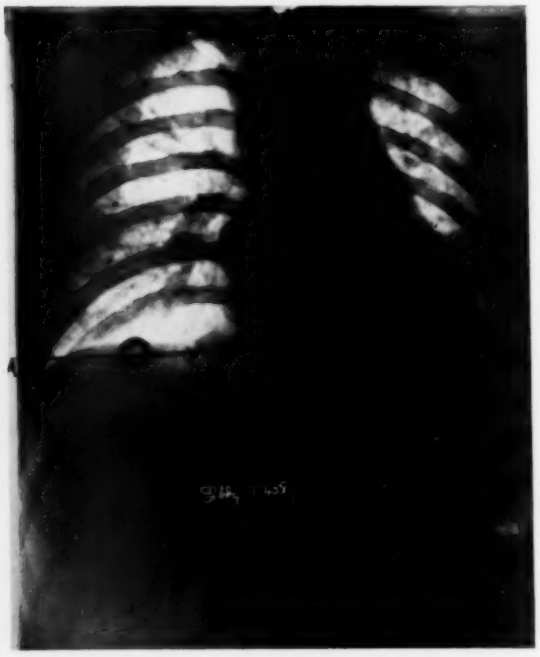


FIG. 13. Case II. Erect anteroposterior roentgenogram made with the Potter-Bucky diaphragm. The foreign body is clearly seen at *A*.

FIG. 14. Case II. Lateral roentgenogram made in the erect posture with aid of the Potter-Bucky diaphragm. Foreign body is seen at *A*, almost superimposed by the lead marker.

another city, and in their studies they diagnosed a foreign body in the right lung. Attempts at removal were made but because of hemorrhage they were discontinued, and the patient was referred to Dr. Gabriel Tucker.

Past medical and family histories have no bearing on the present complaint.

Physical examination (limited to chest) by Dr. O. H. Perry Pepper, was mostly negative. Dr. Pepper thought that there was a small non-obstructing foreign body, left lower lobe with slight compensatory emphysema.

The blood examination, including the blood count and Wassermann reaction, showed nothing abnormal.

The *roentgen examination* of the chest made on December 22, 1930, showed a foreign body.

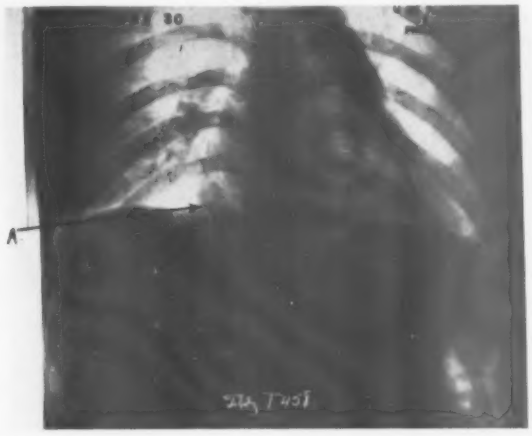


Fig. 15. Case II. Anteroposterior roentgenogram made with the Potter-Bucky diaphragm in the recumbent posture. Foreign body at *A*. The central ray was placed over the midline of the patient's body.

(piece of a tooth) in a right lower lobe bronchus, posterior division (see Fig. 12). There was very little lung reaction around or distal to the foreign body. It was possible to see this foreign body in the erect posture, but with the patient in the recumbent posture it was obscured by the liver (see Figs. 13 and 14, and compare with Fig. 15).

Our plan of localization was the same in this as in Case I. About the only additional procedure utilized was the posteroanterior Potter-Bucky roentgenogram with the patient in dorsal recumbency (bronchoscopic) position. This allows us to duplicate every procedure

Fig. 16. Case II. Anteroposterior roentgenogram with the central ray directed over the localizing markers. Compare this appearance with that seen in Figure 15.

that is used during roentgenoscopic guidance and bronchoscopic removal.

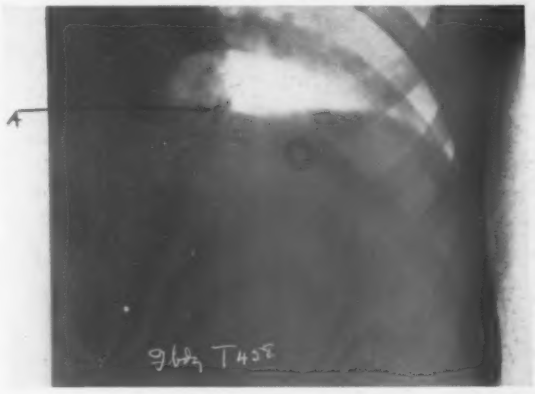


Fig. 17. Case II. Posteroanterior roentgenogram with patient lying on the back and the Potter-Bucky diaphragm above the patient. This gives an absolute record of the position of the foreign body to the markers, as by this method we duplicate the conditions under which the foreign body is to be removed. Foreign body seen at *A*.

FIG. 18. Case II. The foreign body cannot be seen clearly in the lateral view which was made with the patient in the recumbent posture (bronchoscopic position) but can be seen on the original. This illustrates, however, the use of the external markers.

The foreign body was removed bronchoscopically on December 24, 1930, with the aid of roentgenoscopic guidance, and the patient went home on December 25.

SUMMARY

Two cases are reported in which it was previously impossible to furnish roentgenoscopic guidance during attempts at bronchoscopic localization of foreign bodies because the foreign bodies could not be localized roentgenoscopically.

A method that was successfully used in the two chest cases is suggested for aid in localizing the foreign body and assistance during roentgenoscopic guidance in bronchoscopic removal.

Roentgenograms using the Potter-Bucky diaphragm should be made of every obscure and dense lung lesion before excluding foreign bodies.

BRONCHOSCOPY UNDER BIPLANE ROENTGENOSCOPIC GUIDANCE

GABRIEL TUCKER, M.D.

Bronchoscopy with the distally lighted tube under the guidance of direct vision should have no mortality. With local anesthesia in adults, the judicious use of sedatives and adequate training of the bronchoscopist in the proper technique, there should be no result more serious than a temporary discomfort.

Roentgenoscopic bronchoscopy, however, is much more difficult and dangerous, and should be used only when bronchoscopy, by direct vision, cannot accomplish the desired result. Roentgenoscopic guidance should not be allowed to meet the emergency of inadequate training on the part of the bronchoscopist. It should not be attempted unless biplane guidance is available, because safe localization cannot be given without guidance in two planes at right angles, 90°. There must be perfect cooperation between the roentgenologist and the bronchoscopist. Greater skill is required of the bronchoscopist during roentgenoscopic guidance than if he were working by sight. While the roentgenologist is guiding the forceps with relation to the foreign body, a "sense of touch" with the forceps in the hands of the bronchoscopist that comes only with long and arduous practice, is the safeguard for the patient's life, because the large blood vessels are in intimate relation with the forceps and they are not visible under the roentgenoscope. The larger bronchi should always be entered under direct vision through the bronchoscope. The bronchoscopist must also be able to see the roentgenoscopic screen in order to check on the general direction of the manipulation, the finest details of guidance being left entirely to the roentgenologist.

In foreign body cases, when the density of the pathologic tissue in the lung is almost as great as the foreign body, the use of Pancoast and Pendergrass's technique of Potter-Bucky diaphragm and opaque markers makes localization and roentgenoscopic

guidance possible where it would not be possible with ordinary roentgenoscopy.

Roentgenoscopic bronchoscopy should not be attempted on the patient until the bronchoscopist and the roentgenologist have perfected their cooperative technique on the living narcotized animal. Biplane roentgenoscopic guidance has given valuable aid in the diagnosis and treatment of disease in a number of cases where we were unable to aspirate, bronchoscopically, an interlobar collection. Roentgenoscopic guidance by the same technique has enabled us to aspirate through a bronchus that communicated with the collection and evacuate it.

SUMMARY

1. Roentgenoscopic bronchoscopy should be *biplane* and should not be attempted on the patient until the bronchoscopist and the roentgenologist, working together, have perfected their cooperative technique on the narcotized living animal.

2. Because the large blood vessels of the lung are in intimate relation to the field of manipulation in roentgenoscopic bronchoscopy, and are not visible on roentgenoscopic guidance, fatal hemorrhage may result from slight trauma. The patient's life depends on the "*sense of touch*" of the bronchoscopist.

3. Roentgenoscopic guidance by the Pancoast-Pendergrass method has enabled us to remove, with safety, foreign bodies that could not be localized by ordinary methods.

4. Roentgenoscopic bronchoscopy is of value in the diagnosis and treatment of certain disease conditions and the evacuation of cysts and interlobar collections.

AN ORIGINAL METHOD OF ESTIMATING KIDNEY FUNCTION BY MEANS OF THE ROENTGEN-RAY IN INTRAVENOUS UROGRAPHY*

By E. C. CARHART, M.D.
LOS ANGELES, CALIFORNIA

IMMEDIATELY upon the introduction of uroselectan and skiodan into America for use in intravenous urography, I was fortunately in a position to employ this method of roentgen examination of the genitourinary tract. To date no unpleasant symptoms or reactions have occurred other than slight nausea in two cases with vomiting of 2 to 3 ounces of gastric contents in one case; several patients complained of pain in the veins between the elbow and shoulder, the severest pain being at the shoulder only, in most of the cases. Pain was complained of only when perhaps the solution was a little too cold, too warm, or not sufficiently diluted. For some time I have used skiodan exclusively as the intravenous agent; 100 c.c. of a 20 per cent solution is now used in all patients weighing 100 pounds or over. For less than 100 pounds body weight, 1 c.c. of 20 per cent solution per pound is now used.

The literature with reference to skiodan recommends 50 c.c. of a 40 per cent solution (original package concentration and quantity). This concentration, in my experience, has invariably been accompanied by pain in the arm and shoulder as previously mentioned.

The apparatus used consists of 1 platinum needle, two 50 c.c. B-D or Luer syringes, 1 glass adapter, 5 inch rubber connector, 1 beaker (150 c.c.) and rubber tourniquet (Fig. 1).

Films are made with the patient in the horizontal position, 14″×17″ size, one before injection and one immediately, fifteen and thirty minutes after injection has been completed. At the fifteen minute period a second exposure is made with the patient in the upright position. When the kidney function is normal the best definition of the genitourinary tract is usually obtained immediately after the injection is completed.

After much study and many experiments a method of estimating the percentage of skiodan eliminated in thirty minutes has been devised. The skiodan secreted in thirty minutes is hoped to prove to be a direct test of the combined kidney function.

Six flat bottom 20 c.c. test tubes were grouped around a similar central tube and 15 c.c. of 2, 3, 4, 5, 6 and 8 per cent solution of skiodan was placed in the outer tubes, forming a scale or meter as shown in Figure 2. In the central tube of the meter is placed 15 c.c. of skiodan urine (the patient having voided just before the intravenous injection and again at the end of thirty minutes). The skiodan meter (Fig. 2) is then exposed to roentgen rays, using 70 kv., 20 ma., distance, 25 in., time, 15 sec., 5″×7″ Eastman Supersensitive film in folder. The density of the skiodan urine (center) is directly compared with that of the known percentages of skiodan in the surrounding tubes and the percentage of skiodan in the urine thus determined. The thirty minute specimen is measured for quantity and specific gravity. (The specific gravity is made as a matter of record and for possible further comparison and deduction.) It is then a simple mathematical calculation to determine the total thirty minute excretion of skiodan in grams. It is considered that approximately 40 per cent of the skiodan injected intravenously should be eliminated in the urine at thirty minutes after the injection has been completed. To be sure that there is no residual urine in the bladder another film, 8″×10″, is exposed over the bladder area immediately after collecting the thirty minute specimen.

* Received for publication December 2, 1931.

The use of the skiodan meter as described followed unsuccessful attempts at estimation by means of aluminum filters of varying degrees of thickness. It is probable that

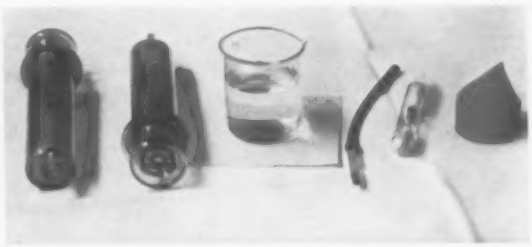


Fig. 1.

aluminum or other metallic meters will be so constructed as to take the place of the author's skiodan meter, but aluminum was not found to be sufficiently flexible for experimental purposes. A slight variation in the diameter of the test tubes was also encountered, but is of no moment provided the depth of the skiodan solutions and that of the skiodan urine is equal in the tubes.

Control experiments were made using phenolphthalein intramuscularly. The two methods corresponded very accurately. The phenophthalein test was a failure when that reagent was combined with skiodan and injected simultaneously.

Intravenous urography is not intended to displace the retrograde method, but is an additional method of examination. Each method has distinct advantages over the other. Among the advantages of intravenous urography can be classed the following:

1. Ease and simplicity of administration
2. Painlessness
3. Usually more speedy
4. Less expensive to patient
5. No after symptomatology
6. Kidney function accurately estimated at the time of intravenous urography.

Should both kidneys and ureters cast equally dense shadows, separate ureteral catheterization is unnecessary. Should considerable variation between the two sides be observed, separate kidney function test by means of cystoscopy should be made. It is my opinion that intravenous urography

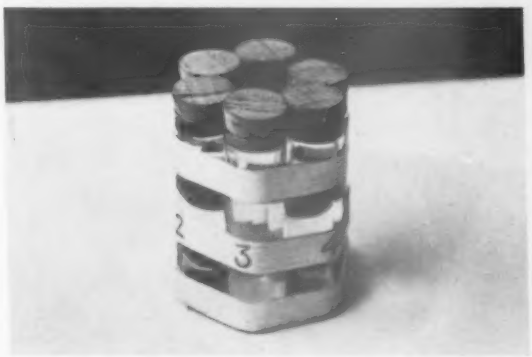


Fig. 2.

should be used routinely in suspected genitourinary disease, much the same as gastrointestinal roentgen examinations are now used in suspected gastrointestinal pathology.

Thankful appreciation is extended to Dr. John J. Burby for valuable and helpful suggestions and assistance.

HISTORICAL DEVELOPMENT OF THE ROENTGEN DIAGNOSIS OF THE PATHOLOGICAL APPENDIX

By JACOB BUCKSTEIN, M.D.
Instructor in Gastrointestinal Roentgenology, Cornell University Medical College
NEW YORK CITY

VARIOUS methods have been devised for determining chronic disease of the appendix, such as localized tenderness at McBurney's point, hyperesthesia in Sherren's triangle, Livingstone's sign, Bastedo's sign and those of Reder and Rovsing. Probably the most concrete evidence, in the absence of a history of an acute classical attack, is that furnished by the roentgen ray.

How important a careful differential diagnosis is before assuming that attacks of pain in the right lower quadrant are due to actual appendicial disease, is indicated in the report of Connell,[13] who found that in 48 out of 212 cases operated on by him, for chronic appendicitis, the results were unsatisfactory; and in the report of Gibson,[19] indicating an unsatisfactory result in 102 out of 426 cases in which a careful follow-up record was obtained.

It is not only in the diagnosis of the chronic appendix as a cause of right lower quadrant pain that difficulty arises, but also in those cases where a pathological appendix has been suggested as the cause of upper abdominal disorders.[9,21,22,25]

Braithwaite[7] showed by injection of the lymphatics, a pathway leading from the appendix to glands in the pyloric region of the stomach.

Moynihan[28] has described vascular engorgement of the pyloric antrum as an occasional finding in disease of the appendix; and Deaver[16] has accused the appendix of being "the high arch perpetrator as a distributor of infection" and "that practically all upper abdominal surgical ailments are primarily due to infection in the appendix, for example, cholecystitis, duodenal and gastric ulcer, multiple abcess of the liver, and a small percentage of chronic pancreatitis."

The common occurrence of changes that may be considered pathological in the appendix, in the absence of any symptoms pointing to appendicial disease, is indicated in the report of Williams and Slater,[33] who studied the condition in 500 laparotomies in patients operated on for other causes. In 167, definite changes in the appendix were present. The finding of such change in the appendix as adhesions, deformities or enteroliths may therefore not constitute sufficient justification for assuming that such an organ is necessarily the cause of any abdominal symptomatology.

The finding of slight adhesions does not justify the diagnosis of chronic appendicitis, since physiologically various membranes may be formed about the appendix which cannot be definitely distinguished from true adhesions.[2]

Connell[14] has stated the perplexing situation as follows:

> Inasmuch as it is difficult to gauge the extent of the pathology in chronic appendicitis from the symptoms, before the abdomen is open, as it is still difficult from the gross pathology after the abdomen is opened and the organ is palpated and inspected; and as it is still difficult from the histo-pathology after the appendix has been removed and subjected to microscopic study, one may anticipate a certain degree of complexity and difficulty in a study of the subject of chronic appendicitis. A condition that is among the most difficult to diagnose within the entire list of surgical diagnoses, but one which is made everywhere, every day, by everybody, with as much nonchalance and much less evidence than is called to one's support in commenting upon the weather. One might say of this condition that it is the most treated and the least diagnosed surgical disease. In the authoritative text books and treatises upon the subject of appendicitis, one finds hundreds of

pages devoted to *acute appendicitis* with often less than a proportionate number of lines, at most paragraphs devoted to the subject of *chronic appendicitis*, while in every hospital in the United States hundreds of chronic appendicitis cases are being operated upon to one acute case.

In 1909, Béclère[5] reported his experience with a patient whom he had roentgenographed three years previously, in which case he succeeded in clearly demonstrating the bismuth-filled appendix. He predicted that with improvement in technique, such roentgenographic visualization of the appendix would be frequently made, and would prove to be of considerable practical value, by indicating its exact position, and in cases where the diagnosis of a pathological appendix was in doubt, one might show whether the point of tenderness elicited on pressure, coincided with the position of the visualized appendix.

Liertz[27] showed that such demonstration of the appendix was technically possible.

In one case in which Liertz succeeded in doing so, operation was performed, and a chronically diseased appendix was removed which corresponded exactly in its anatomical position to the position noted in the roentgenogram. By serial roentgenograms he was able not only to study the filling of the appendix with contrast substance but the gradual emptying as well.

Desternes[17] reported his roentgenographic findings in a young man nineteen years of age, with recurring attacks of pain in the right lower quadrant. He showed that by means of this method evidence could be obtained regarding the size, shape and presence of fixation of the appendix. This was confirmed by surgical intervention. He moreover called attention to the fact, that the roentgenographic method might be of service in a doubtful case through elimination of the appendix as a cause by demonstrating the presence of a lesion in some other organ.

The value of clearly differentiating the various possible causes of right lower quadrant pain was later emphasized by Kantor.[24]

The importance of localized tenderness over the appendicial area in the diagnosis of the pathological appendix, even though the appendix itself might not be roentgenologically demonstrable, was emphasized by Singer and Holzknecht.[31] In such cases the position of the appendix was presumed from the position of the cecum.

Such failure of visualization of the appendix may, however, be due to the fact that it is empty of contrast substance at the time, although filled at other times. As Cohn[11] has indicated, the emptying is due to peristaltic movements.

The segmented appearance of the appendix may simply be evidence of activity similar to the haustral segmentation of the colon, and interpretable as an entirely normal phenomenon.[12]

White[32] has also called attention to the normal nature of the segmented or beaded appearance of the appendix. Its functional nature is indicated by the fact that it is never found at autopsy or operation.

Failure of the appendix to fill may also be due to actual obliteration of the lumen. In subacute appendicitis, the appendix may fail to fill because it is in an inflamed condition as Baetjer and Friedenwald[3] have emphasized. In that event tenderness over the appendicial area under roentgenoscopic control even though the appendix itself is not visible, may be the only roentgenologic evidence obtainable suggesting a pathologic state.

Groedel[20] came to the unwarranted conclusion that the normal appendix could not be demonstrated roentgenologically. He contradicted the observations particularly of French authors that they had frequently noted the normal appendix by means of the roentgen ray, as due to incorrect differentiation from filled portions of the small intestine. He assumed that only the pathological appendix was demonstrable, and then only rarely so.

Case, in 1912, reported before the American Roentgen Ray Society 60 cases in which the appendix was visualized. In 1914, he summarized his experience in 325 cases of

visualized appendices.[10] The examination should be conducted roentgenoscopically in the horizontal position, with manual palpation to separate the appendix and bring it into clear relief. The importance of localized tenderness is particularly emphasized as an evidence of pathology. A poorly draining appendix which retains the contrast substance for many days is potentially pathological, since it may be presumed that pathogenic bacteria similarly retained may prove dangerous.

Alwens[1] has similarly emphasized the predisposition to inflammatory disease of an appendix which remains visible for too long a time.

That a normal appendix may be readily demonstrable by the roentgen method was shown by George and Gerber,[18] who verified the fact in many cases, when abdominal surgery was performed for other conditions. Similarly Rieder[30] in a later article reversing his original opinion demonstrated filling of the appendix under normal conditions. He described active contractions with change of position of the appendix, and occasional deep constrictions similar to intestinal segmentation. It is emptied by peristaltic activity. While the appendix can fill only when the lumen is not destroyed, failure to fill does not necessarily indicate that the lumen is obliterated.

Under pathologic conditions, the visualized appendix may be abnormal in position or shape. Tenderness on pressure over the appendix under roentgenoscopic control is significant. Enteroliths, may be demonstrable. Ileal stasis at twenty-four hours and longer may be a concomitant finding as well as stagnation in the appendix itself.

Stereoroentgenography in the study of the visualized appendix has been recommended by Imboden[23] for the determination of its true direction, and the demonstration of kinking.

The significance of the roentgen evidence in the diagnosis of disease of the appendix was emphasized by Pfahler,[29] particularly with regard to localized tenderness, fixation, position, angulation, constriction and abnormal retention. Lichty[26] corroborated the clinical value of such diagnostic evidence.

Cambies[8] has recommended the admixture of magnesium chloride with the barium preparation, as an aid in the more frequent visualization of the appendix, and Czepa[15] to accomplish this purpose recommends the administration of a barium-epsom salts mixture in the morning, followed by a barium meal the same evening. The appendix is examined on the following morning. About two teaspoonsful of salt is administered in the average patient.

Béclère[4] in 1902 envisioned the remarkable future of gastrointestinal roentgenology as the result of the method of introducing large quantities of a suspension of bismuth into the stomach. In 1909 he showed the applicability of the method to the visualization of the appendix.[5] Moreover, with great insight he discerned what is still the essential contribution of the roentgen method in the diagnosis of appendicial pathology, namely, tenderness localized to the visualized appendix itself.

REFERENCES

1. ALWENS. Die Darstellung der Appendix im Röntgenbild. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921–1922, *28*, 264–265.
2. ASCHOFF, L. Pathogenes und Aetiologie der Appendicitis. *Ergeb. d. inn. Med. u. Kinderh.*, 1912, *9*, 1–29.
3. BAETJER, F. H., and FRIEDENWALD, J. Roentgenological aspects of lower right quadrant disease. *Tr. Am. Gastro-Enterol. Ass.*, 1920, 193–207.
4. BÉCLÈRE. La radioscopie et la radiographie des organes splanchniques. *Arch. d'électric. méd.*, 1902, *10*, 624–660.
5. BÉCLÈRE. Presentation d'un radiogramme montrant sur le vivant l'image de l'appendice iléo-caecal. *Bull. et mém. Soc. de radiol. méd. de Par.*, 1909, *1*, 192–195.
6. BELOT, J. Radiographie d'appendice vu a l'examen radioscopique. *Bull. et mém. Soc. de radiol. méd. de Par.*, 1911, *3*, 326–328.

7. Braithwaite, L. R. Flow of lymph from ileocaecal angle and its position bearing on cause of duodenal and gastric ulcer. *Brit. J. Surg.*, 1923, *11*, 7–26.
8. Cambies. New method for radiologic examination of the appendix; its application to the diagnosis of chronic appendicitis. *Progrès méd.*, 1926, *54*, 263.
9. Carnett, J. B., and Boles, R. S. Fallacies concerning chronic appendicitis. *J. Am. M. Ass.*, 1928, *91*, 1679–1683.
10. Case, J. T. Roentgen examination of the appendix. *N. York M. J.*, 1914, *100*, 161–167.
11. Cohn, M. Der Wurmfortsatz im Röntgenbilde. *Deutsche med. Wchnschr.*, 1913, *39*, 606–608.
12. Cohn, M. Zur Frage der Beweglichkeit und Bewegung des Wurmformsatzes. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1928, *38*, 26–38.
13. Connell, F. G. Pseudo-appendicitis. *J. Am. M. Ass.*, 1916, *67*, 335–337.
14. Connell, F. G. Chronic appendicitis, so-called. *Med. Rec.*, 1921, *99*, 214–218.
15. Czepa, A. Weitere Beiträge zur Röntgendiagnostik der Appendix. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1929, *40*, 214–241.
16. Deaver, John B. Appendicitis. *J. Am. M. Ass.*, 1928, *90*, 1679–1683.
17. Desternes. Radiographie de l'appendice ileocaecal; observation nouvelle contrôlée par l'intervention chirurgicale. *Bull. et mém. Soc. de radiol. méd. de Par.*, 1911, *3*, 323–326.
18. George, A. W., and Gerber, I. The value of the roentgen method in the study of chronic appendicitis and inflammatory conditions, both congenital and acquired about the cecum and terminal ileum. *Surg., Gynec. & Obst.*, 1913, *17*, 418–427.
19. Gibson, C. L. The results of operations for chronic appendicitis; a study of 555 cases. *Am. J. M. Sc.*, 1920, *159*, 654–663.
20. Groedel, F. M. Die röntgenologische Darstellung des Processus Vermiformis. *München. med. Wchnschr.*, 1913, *60*, 744–745.
21. Held, I. W., and Goldbloom, A. A. Differential diagnosis of peptic ulcer and chronic appendicitis. *Am J. Surg.*, 1930, *10*, 274–284.
22. Heyd, C. G. Mimicry of gastroduodenal ulceration by disease of the appendix, with remarks on the lymphatic drainage from the ileocecal region to the upper abdomen. *Tr. Am. Gastro-Enterol. Ass.*, 1924. Also *M. J. & Record, Suppl.*, 1924, *120*, 97–101.
23. Imboden, H. M. Roentgen diagnosis of lesions of the vermiform appendix. Am. J. Roentgenol., 1915, *3*, 581–587.
24. Kantor, J. L. On five common clinical types of appendicitis. *M. Clin. N. America*, 1922, *5*, 1081–1112.
25. Larimore, J. W. Chronic appendicitis; its diagnosis and relation to other abdominal diseases. *South. M. J.*, 1930, *23*, 354–359.
26. Lichty, J. A. Chronic appendicitis. *J. Am. M. Ass.*, 1922, *79*, 887–893.
27. Liertz, R. Die radiographische Darstellung des Wurmformsatzes. *Deutsche. med. Wchnschr.*, 1910, *36*, 1269–1270.
28. Moynihan, B. Gastric ulcer and its treatment. *Med. Rec.*, 1921, *99*, 903.
29. Pfahler, G. E. The roentgen rays in the diagnosis of appendicitis. *Tr. Am. Gastro-Enterol. Ass.*, 1918, 83.
30. Rieder, H. Zur Röntgenuntersuchung des Wurmformsatzes, besonders bei Appendizitis. *München. med. Wchnschr.*, 1914, *61*, 1492–1494.
31. Singer, G., and Holzknecht, G. Roentgenologic basis for the diagnosis of chronic appendicitis. *München. med. Wchnschr.*, 1913, *60*, 2659–2664.
32. White, F. W. The clinical importance of chronic changes in the appendix. Am. J. Roentgenol. & Rad. Therapy, 1925, *13*, 12–21.
33. Williams, J. T., and Slater, R. Condition of appendix in 500 laparotomies on patients presenting no symptoms of appendicitis. *Ann. Surg.*, 1919, *70*, 535.

SMALL RADIUM NEEDLES VERSUS RADON IMPLANTS*

By CHARLES L. MARTIN, E.E., M.D.
Associate Professor of Radiology, Baylor University
DALLAS, TEXAS

THE efficacy of multiple small sources of radiant energy placed within tumor tissue is now well established in radiation therapy. However, techniques vary considerably in different parts of the world. After Failla[4] developed the gold radon seed in 1926 it was adopted by almost all of the large American institutions, particularly those located near New York City. Since implants of this type can only be produced in practical quantities in establishments owning large amounts of radium and enjoying the services of a trained physicist having available expensive refining apparatus, radiologists situated in the more remote portions of the United States have found the use of seeds rather unsatisfactory. The commercial companies have, it is true, attempted to solve this problem by making airplane deliveries in relatively short periods of time, but radon obtained in this way is often too expensive to fall within the reach of many of the patients that need it most.

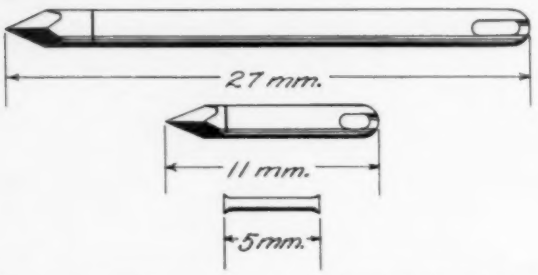


FIG. 1. Drawings made to scale showing the relative sizes of weak platinum radium needles advocated by Cade and a gold radon seed. The large needle is 27.0 mm. long, 1.85 mm. in diameter, contains 1.33 mg. of radium and has a wall thickness of 0.6 mm. The small needle is 11.0 mm. long, 1.5 mm. in diameter, contains 0.6 mg. of radium and has a wall thickness of 0.5 mm. The gold seed is 5 mm. long, 0.75 mm. in diameter, usually contains 1.0 to 2.5 millicuries of radon and has a wall thickness of 0.3 mm.

In an effort to overcome this difficulty we have looked about for a worthy substitute for radon implants and believe that the highly filtered radium element needles advocated by the English radiotherapists, Evans and Cade[3] and Birkett[1] not only produce equally good results but are in some ways superior to gold seeds. The plan of treatment is based on the principles laid down by Regaud[11] who advocates heavy filtration, small sources of energy and long periods of irradiation.

TECHNIQUE

The needles are made of platinum and may be of any length but are constructed so as to contain approximately 0.6 mg. of radium element per running centimeter of over all length. At the present time we are using only two sizes, one containing 0.6 mg. of radium and measuring 11.0 mm. in length and one containing 1.33 mg. and measuring 27 mm. in length, as illustrated in Figure 1. The small needles have a wall thickness of 0.5 mm. whereas the walls of the larger ones measure 0.6 mm. This type of filtration eliminates beta radiation and reduces the reaction around the needles to a minimum. The calculation of dosage is

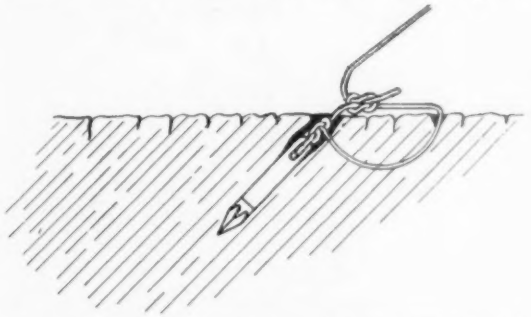


FIG. 2. Drawing illustrating the method used in suturing radium needles in the soft tissues of the mouth. The long end of the suture passes out of the mouth and is tied to a radium tag strapped to the face.

*Read at the Thirty-second Annua Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22-25, 1931.

relatively simple since 0.6 mg. of radium in such a needle causes the complete disappearance of a cubic centimeter of squamous cell carcinoma if the applicator is left in the center of the mass of tissue for seven days. Needles are therefore spaced at 1 centimeter distances when they are placed in position. In parts of the body where motion is likely to take place, as in the mouth, it is necessary to fasten each needle in the tissues with a suture so that it cannot move. This procedure is carried out under strict aseptic precautions using local anesthesia. Heavy waxed dental floss is used for suture material and the sutures are placed in accordance with Cade's[2] technique as illustrated in Figure 2. One end of each suture is not cut off but extends outside the mouth where it is tied through the eye in a radium tag strapped to the patient's forehead. Fourteen or fifteen platinum needles may be worn in the tongue, floor of the mouth or cheek for seven days with surprisingly little discomfort. At the end of the seven days the sutures are cut and the needles are removed. When implantations are made in surgical wounds or in tumors of the bladder, prostate or breast, it is not necessary to employ sutures.

Implanted tumors begin to shrink soon after the needles are removed but sloughs are never observed and painful reactions are not produced. In the mouth a whitish membrane appears over the treated area in about ten days. The tumor melts down beneath the membrane which slowly disappears, and in six to eight weeks the involved area is covered over by normal epithelium and only a slight amount of superficial scarring can be made out. Careful palpation of the tissues reveals practically no fibrosis and there is an almost complete restoration of function. This type of healing is most desirable in lesions of the tongue where a good functional result is of the greatest importance.

In using this method an effort is always made to surround the lesion with needles placed in the adjoining normal tissues. We have been able to duplicate some of the excellent results in cancer of the breast reported by Keynes,[7] in cancer of the rectum reported by Gordon-Watson[5] and in cancer of the bladder reported by Cade, using this principle.

Recently certain claims for the superiority of gold seeds have been published which are not entirely in line with our experience. For this reason the remainder of this paper will be devoted to a discussion of the advantages and disadvantages of the two methods. All comparisons are made between the needle technique just described and the gold implant technique now in use at the Memorial Hospital in New York.

DISADVANTAGES OF RADIUM NEEDLES

In our experience the needles have only one serious disadvantage, namely, the fact that they cannot be used in inaccessible places such as the posterior portion of the tongue, the epiglottis, the posterior nasopharynx, etc. Radon seeds may be successfully planted through special applicators in these regions. Fortunately tumors in such locations are relatively rare and needles may be utilized in the majority of the patients who apply for treatment.

Martin and Sharp[8] allow many of their patients to return home immediately after the implantation of gold seeds and point to the hospitalization for seven or eight days necessary with the needle therapy as a serious drawback. Their criticism applies only to intraoral cases but even these patients are given an excellent start toward recovery when they remain in an institution for a time, receive a proper diet and are shown how to carry out the hygiene needed with a diseased mouth. It is also possible to execute a careful plan of irradiation of the adjacent lymphatics with radium packs and deep roentgen therapy during the same period, so that the whole treatment may be carried out in a reasonably short time and considered as a unit which need not be repeated for a long in-

terval, if at all. Patients who come from a distance find this plan most advantageous.

Even the smallest needles have about twice the length and twice the diameter of the gold seeds and this bulk has been pointed out as a great disadvantage. However, such has rarely proved to be the case in practice. We have successfully implanted 11.0 mm. needles in the mucous membrane of the hard palate and alveolar margins and believe that the extra filtration more than compensates for the bulk when the implants are placed near bony structures. Portions of the tumor that cannot be properly implanted may be treated with 25 and 50 mg. platinum radium capsules held against the involved regions by lead strips as advocated by Grier,[6] Pfahler,[9] and Widmann.[13]

ADVANTAGES OF RADIUM NEEDLES

In my opinion the disadvantages of the needles are far outweighed by their advantages, and their merits are well sustained when a comparison is made with radon seeds.

At the outset I wish to state that the needle advocated in this paper appears to be more efficient than the radon implant. This statement is made with a full knowledge of the following quotation from the recent paper of Martin and Sharp relative to radium needles: "This method of placement is extremely inefficient since at least three-quarters of the energy is directed away from the tumor and therefore never reaches it. For this reason the total dosage must be larger and as a consequence there is a needlessly severe reaction in adjacent normal tissue as well as a greater chance of slough." First let us consider only the matter of efficiency. Martin and Sharp state that the minimum dose of radiation delivered by the gold seed that will completely destroy squamous cell carcinoma amounts to 7 erythema doses. According to the recent work of Quimby and Stewart,[10] a gold seed left permanently in the tissues must contain 1.4 millicuries when it is implanted if it is to deliver 7 erythema doses to a mass of tissue 1.0 cm. in diameter. The total dose used is therefore the equivalent of 186.2 mg-hr. Now it has been shown that a small platinum needle containing 0.6 mg. of radium element will destroy a mass of carcinoma 1.0 cm. in diameter if the needle be left in place for seven days. The dosage used here is 100.8 mg-hr. and since the filtration is almost twice that used with the seed there is no sloughing produced. The result is brought about with a little more than half the total energy utilized by the radon implant. The plan of placing this type of needle in the normal tissue outside the tumor produces no slough or other ill effects and concentrates the dose just beyond the growing edge where it is most needed. Even though the total number of needles used is twice the number of implants that might be needed for a given tumor, the total dosage is about the same and the total area irradiated is much larger.

It has been claimed that element needles should be more efficient than radon sources because the intensity of radiation is constant and does not rapidly diminish as it does with radon. This explanation is, of course, entirely theoretical and may not be a correct one.

Perhaps the greatest attribute of the radium needle is its high filtration. Six-tenths milligram of radium filtered through 0.5 mm. of platinum may be left in the tissues for seven or eight days without the production of a slough or even a really painful reaction, and this statement applies to the membranes lining the mouth, bladder, rectum, etc., as well as to the more radioresistant structures. The 0.3 mm. gold filter used in implants does not remove all of the beta rays, 8.8 per cent of the total radiation passing through it being of the beta variety. This seems like an almost negligible quantity but nevertheless I have obtained some rather severe and very painful sloughs in the tongue with 1.5 millicurie implants. Gold seeds when placed in direct contact with bone, as about the

alveolar margins and against the hard palate, are likely to set up a rather painful destructive process sometimes spoken of as radiation osteomyelitis which may require surgical treatment. The highly filtered 0.6 mg. needles have been placed in contact with the bony processes and have not produced any demonstrable bone complications. Such a freedom from reaction is also highly desirable when it is necessary to use radium near the eyeball or the cartilages of the ear or nose.

Much has been said about the ease with which implants can be placed but accuracy is really much more important than ease of manipulation. If a number of seeds are to be used nothing remains to mark their locations after they are inserted, and their exact relation to one another can easily be confused. With the needles a suture and a guy thread marks each point of implantation so that a very even distribution is possible. Should a needle be sewn in a disadvantageous position it may be removed

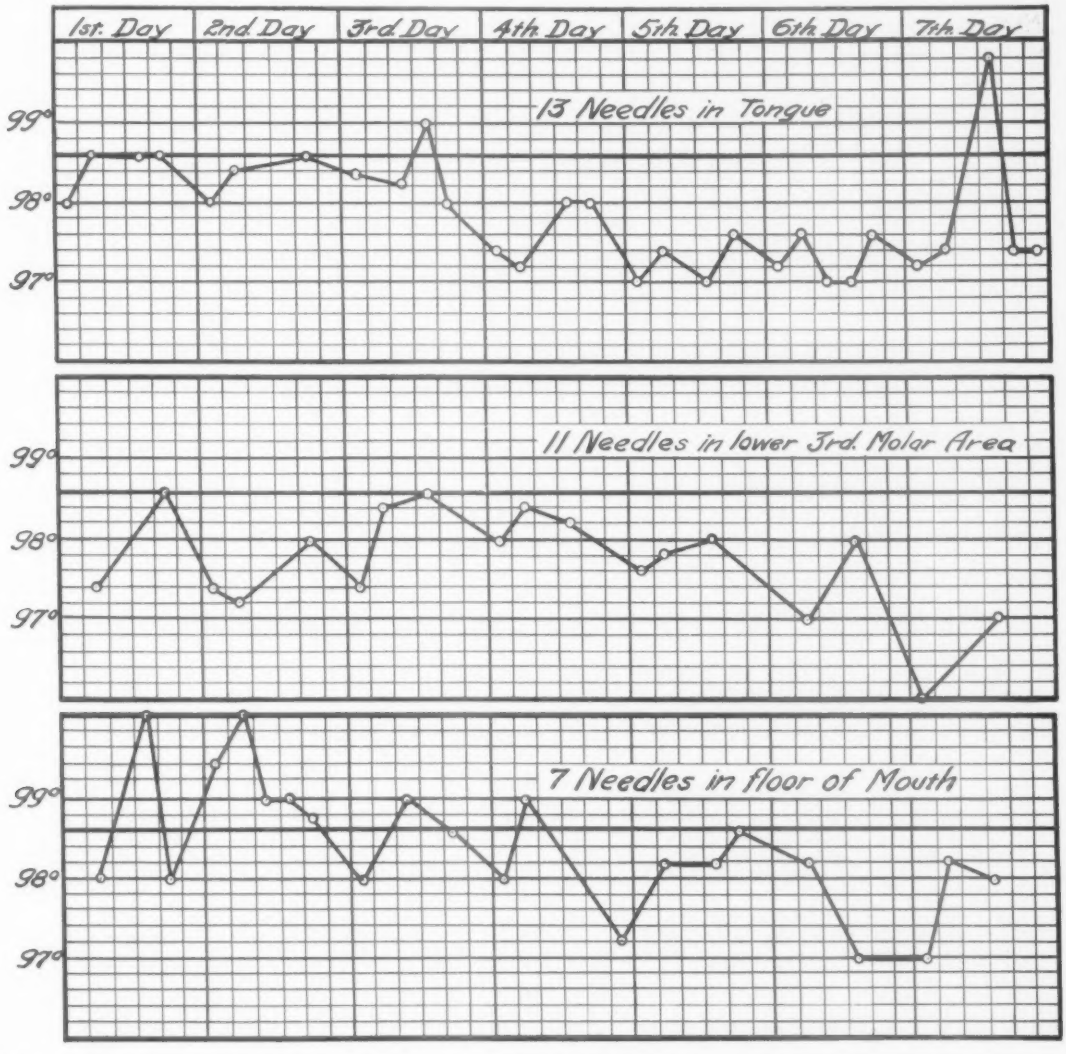


Fig. 3. Three temperature charts picked at random from our series covering the seven days of hospitalization required of the intraoral cases having radium needles sewn in the mouth. Only slight intermittent temperature elevations are noted and subnormal temperatures are common because the patients are usually old and inactive.

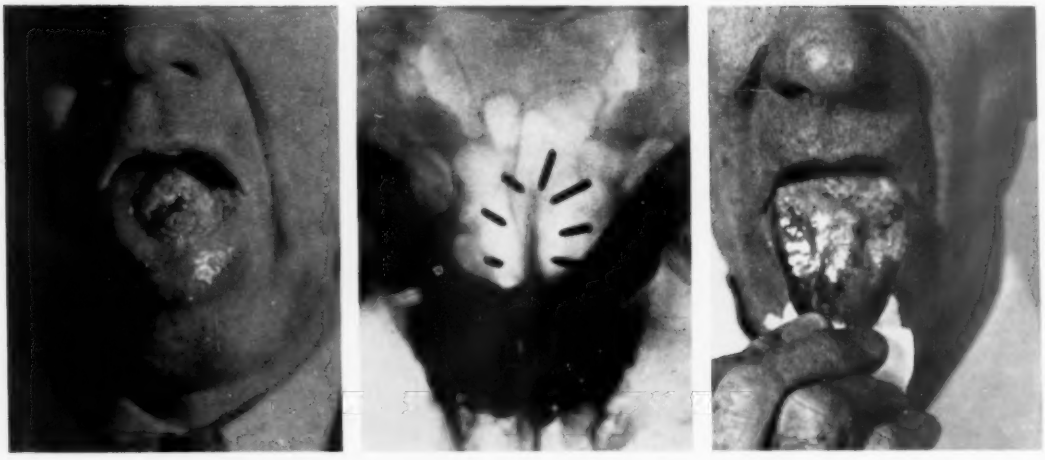


Fig. 4. Squamous cell carcinoma of the tongue of five months' duration treated by the implantation of nine 0.6 mg. platinum radium needles around the tumor, as indicated in the roentgenogram, for a period of seven days. The photograph on the right was made fifteen months later, at which time healing was complete and the tongue was soft and pliable. There was no slough and very little discomfort at any time.

and reinserted in its proper place. Following the operation roentgenograms are made of the field and if the spacing is not correct a readjustment can always be carried out. However, when the seeds once leave the trocar their positions are fixed and they cannot be changed.

Another point that must be considered is the fixation of the source of radiant energy, particularly near moving parts, as in the mouth. Needles are inserted through normal tissue so as to surround and pass under the tumor and are held in place by sutures which pass well out into the tough normal tissue. These sutures rarely pull out during an irradiation period of seven days, but when such a mishap does occur the needle cannot be lost because it is securely fastened to a thread tied through a tag strapped to the face. Since the patient

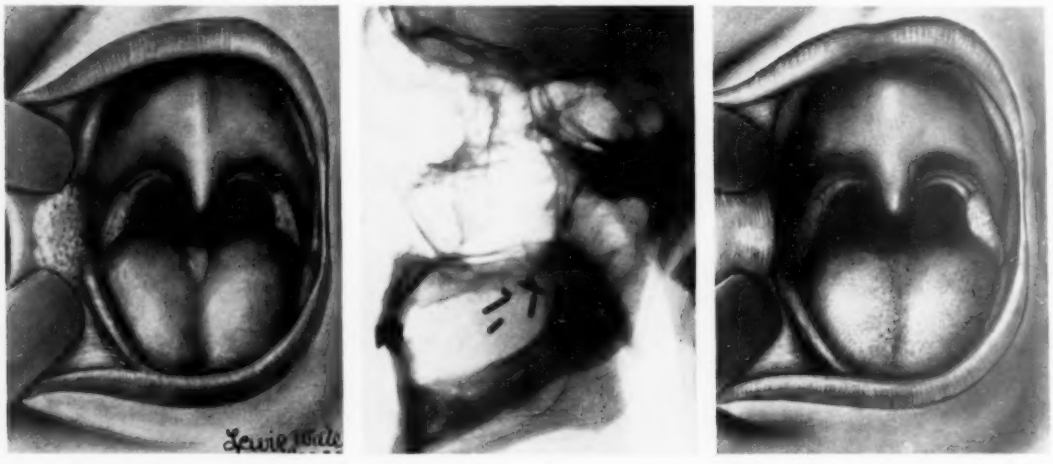


Fig. 5. Squamous cell carcinoma of the right cheek treated by the implantation of seven 0.6 mg. platinum radium needles beneath the tumor, as shown in the roentgenogram, for a period of seven days. The drawing on the right shows the cheek as it looked a year later. There was a slight amount of superficial scarring present but the tissues were soft and the treatment had interfered in no way with opening and closing the mouth.

is in the hospital the needle may be replaced within a reasonable time and the original plan of treatment is not interfered with. Implants, on the other hand, are very small structures which are placed in tumor tissue. This tissue is often soft, friable and partially necrotic, and implants may slip out unnoticed and be swallowed with food. A more unfortunate accident which has happened at least once to my knowledge is the aspiration of the seed during sleep and the subsequent formation of a lung abscess.

first twenty-four hours, but it is most unusual for the patient to have any rise in temperature thereafter. For two or three days preceding the operation the mouth is thoroughly washed out with chartex or some other good antiseptic after each meal. The lesion is then painted with 2 per cent mercurochrome by the patient or some member of his family. Just before the needles are inserted the inside of the mouth is carefully painted with iodine. Following the implantation, the chartex-mercurochrome medication after each meal is re-

Fig. 6. Squamous cell carcinoma of the left lower jaw. This tumor arose in the molar region and extended up onto the cheek and down under the tongue. Nine 0.6 mg. platinum radium needles were planted around the edges of the lesion, as shown in the roentgenogram, for a period of seven days. The photograph on the right was made at the end of six weeks, at which time the lesion had completely disappeared and its site was marked by some superficial scarring which produced no symptoms of any sort. There was no sloughing observed at any time.

Martin and Sharp are much concerned about infection in intraoral cases and state: "The introduction of infection and the occurrence of gross slough is undoubtedly more common in the use of needles than seeds." Such may be the case with the type of needles used by these authors. However, the English needles do not produce a slough and when a proper technique is followed, infection has proved to be a negligible factor in our cases. A few typical temperature charts covering the seven days of hospitalization are reproduced in Figure 3. Where extensive needling is done there may be a slight elevation during the sumed and is continued until healing takes place. Since most mouths containing malignant lesions are infected, this plan is helpful even when no radiation is used. Waxed dental floss makes a soft, painless suture which acts as a drain for the puncture wound. The chance of carrying infection into the tissues is not great because the insertion of the needle and the placing of the suture are carried out in normal uninfected tissue.

After the needles are removed no foreign bodies are left in situ whereas the small gold capillary radon tubes remain permanently in the tissues. The ill effects of such

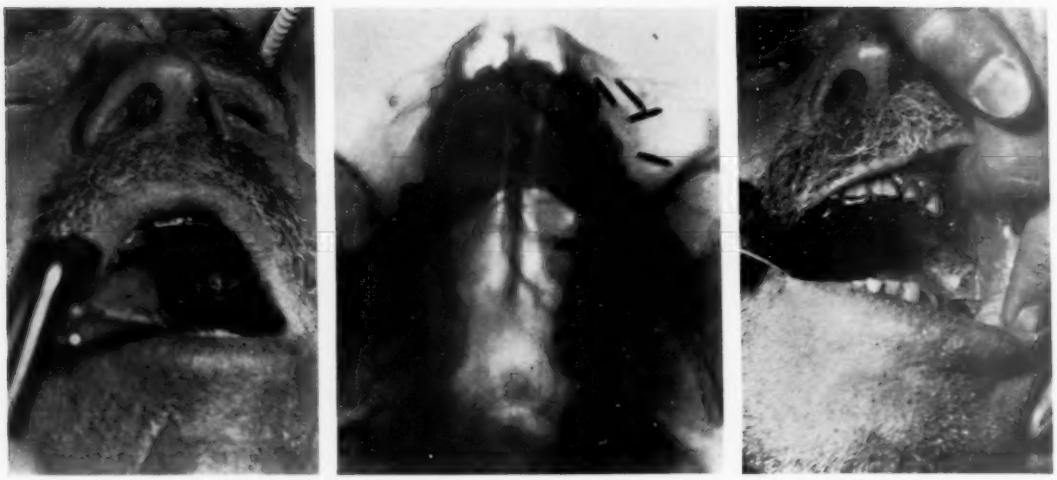


FIG. 7. Large squamous cell carcinoma (grade 1) involving the posterior quadrant of the hard palate on the left side and extending across the alveolar process well out onto the cheek. Eleven 0.6 mg. platinum radium needles were planted under the edges of the lesion, as shown in the roentgenogram, for seven days, and one 50 mg. platinum radium capsule with a wall thickness of 1.0 mm. was held against the center of the lesion for eight hours. The photograph on the right was made seven weeks later. At that time no evidence of carcinoma could be made out and the site of the lesion was replaced by a slightly depressed whitish scar. The patient had no pain or discomfort of any sort.

foreign bodies have probably been exaggerated. However, it is desirable to return the structures surrounding a maligant tumor to as near a normal condition as possible, and the absence of foreign bodies is a point in favor of the needle technique.

The greatest objection raised by both laymen and physicians when they first

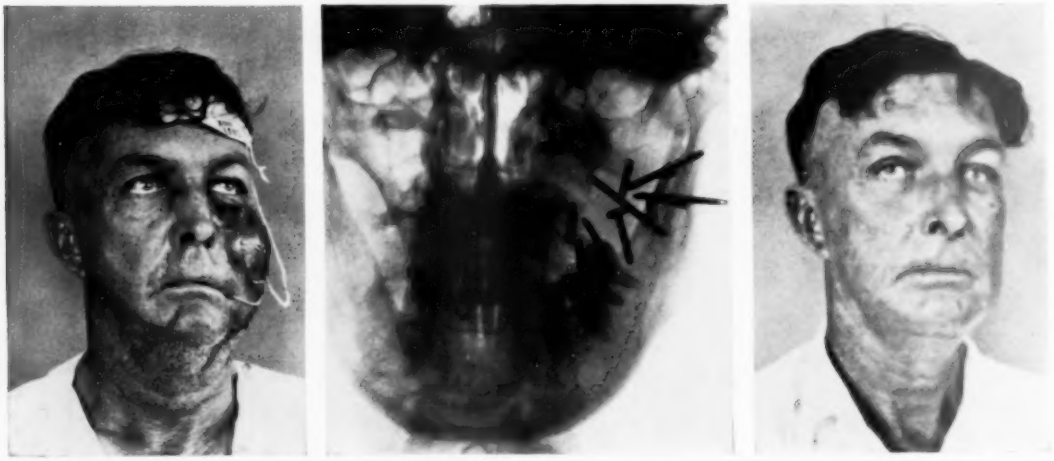


FIG. 8. Far advanced squamous cell carcinoma of the left antrum. The sinus was filled with malignant tissue which had completely destroyed the anterior wall and had extended through the hard palate into the mouth. A malignant lesion about 1 inch in diameter was seen in the roof of the mouth on the left side. Eight 0.6 mg. platinum radium needles were sewn under the edges of the tumor in the mouth and six long 1.3 mg. needles and three 0.6 mg. needles were placed deep in the tumor of the antrum through small incisions made in the skin, for a period of eight days. The photograph on the right shows the same patient six weeks later at which time he was markedly improved. No pain, discharge or slough followed this procedure. A deeper implantation is now indicated and can easily be carried out.

hear of the method is their fear of the pain produced by so many large metallic objects buried in the tissues, particularly in the mouth. I must confess that I had the same reaction when reading a description of Regaud's original technique for treating cancer of the tongue. Pain has not, however, proved to be a troublesome factor and none of the patients require opiates after the first day. Most of them have accustomed themselves to the presence of a lesion in the mouth and state that the presence of the radium needles makes little difference in the sensations that they experience. They take soft and liquid food freely, beginning immediately after the operation, with little difficulty. When the implantations are made well back in the mouth near the anterior pillars swallowing may be somewhat painful but not enough to interfere with the taking of food.

CONCLUSIONS

1. Small heavily filtered platinum radium element needles can be used in all parts of the body that are readily accessible, or can be made accessible by surgery, as an efficient substitute for gold radon implants.

2. Although the use of the needles requires hospitalization they are more efficient than radon seeds. They produce no slough and only a slight reaction, and can be planted with the greatest accuracy. They cannot be lost or aspirated and do not remain in the tissues as foreign bodies. Recovery is rapid and the end-results are remarkably free from complications.

REFERENCES

1. BIRKETT, G. E. Radium treatment in carcinoma of the mouth and tongue. *Lancet*, 1928, *1*, 953–959.
2. CADE, S. Radium Treatment of Cancer. William Wood & Co., New York, 1929.
3. EVANS, A., and CADE, S. Cancer of the tongue. *Brit. J. Surg.*, 1927, *15*, 55–70.
4. FAILLA, G. The development of filtered radon implants. AM. J. ROENTGENOL. & RAD. THERAPY, 1926, *16*, 507–525.
5. GORDON-WATSON, C. Radiation in treatment of cancer of the rectum with radium by open operation. *Proc. Roy. Soc. Med.*, 1927 (*Surg. Sect.*), *21*, 9–19.
6. GRIER, G. W. The treatment of malignant diseases in the mouth. AM. J. ROENTGENOL. & RAD. THERAPY, 1924, *12*, 347–352.
7. KEYNES, G. Radium treatment of primary carcinoma of the breast. *Lancet*, 1928, *2*, 108–111.
8. MARTIN, H. E., and SHARP, G. S. The use of gold filtered radon implants in the treatment of intraoral cancer. AM. J. ROENTGENOL. & RAD THERAPY, 1931, *26*, 28–38.
9. PFAHLER, G. E. Improved technique for the use of highly filtered gamma rays in the treatment of cancer of the mouth. AM. J. ROENTGENOL. [illegible] 1930, *23*, 633–638.
10. QUIMBY, L. H., and STEWART, F. W. Comparison of various sources of interstitial radiation. *Radiology*, 1931, *17*, 449–470.
11. REGAUD, C. Radiotherapy of cancer of the tongue. *Paris méd.*, 1921, *11*, 265–271.
12. REGAUD, C. On curietherapy of the epitheliomata of the tongue and of their following adenopathy. *Brit. J. Radiol.*, 1925, *30*, 361–367.
13. WIDMANN, B. P. Radiation technic for cancer of the mouth with combinations of gamma radium rays and varying quantities of high voltage roentgen rays. *Radiology*, 1930, *14*, 197–206.

DISCUSSION

DR. G. FAILLA, New York City. There is little I can say in the discussion of Dr. Martin's paper, since most of the points brought out are of a clinical nature. I think that Dr. Charles Martin and Dr. Hayes Martin do not mean the same thing when they talk about the relative efficiency of gold implants and radium needles.

I believe that the same distribution of radiation within a tumor may be obtained equally well with gold implants and radium needles. This is evident when one considers that gold implants may readily be placed in the tissue one after the other along a straight line, thus occupying continuously the same space that a long radium needle would occupy. We have developed special implant inserters which permit this without the necessity of repeated punctures. Several of these inserters may be placed in the tumor before any implants are discharged, in order to facilitate the distribu-

tion of the implants. But in addition to being able to duplciate the distribution attainable with radium needles, the implants possess the advantage of greater flexibility, since they are small in size and need not be removed later.

The question of the amount of necrosis produced by the two methods of interstitial irradiation is intimately connected with the distribution of the sources. I do not think that the small amount of beta radiation passing through 0.3 mm. of gold is responsible for the sloughing mentioned by Dr. Martin. On the other hand, the radium or radon content per centimeter is very important. No comparison of the necrosis produced, even by two radium needles, is justified if the lengths of the radiating portions are very different while the total radium content is the same in both. The shorter one will undoubtedly produce more necrosis locally. Of course, this is what happens when a few strong implants are used. But if the required total dose in millicuries is distributed over a large enough number of implants, the tissue reaction should be about the same whether gold implants or radium needles are used.

It should be noted, however, that in treating bulky tumors it is obviously more expeditious to insert a small number of long radium needles than a large number of gold implants. Accordingly the best arrangement is to have both available.

DR. MARTIN (closing). In closing, I merely want to say that Dr. Failla is probably right in asserting that Dr. Hayes Martin and I are talking about two different types of therapy. As regards efficiency, it is certainly logical to assume that the method which produces the desired result with the smallest amount of energy is the most efficient. If my calculations are incorrect, I will be most happy to have Dr. Failla explain my errors.

HEMANGIOMA

SOME OBSERVATIONS ON THE RESULTS OF RADIATION THERAPY*

By HUGO ROESLER,† M.D.

THE indications for and the methods of treating hemangioma vary with the patient and with the location of the lesion. Much depends upon its size, the age of the patient, the probable cosmetic results and the possibility of bleeding.

MATERIAL

This report is based on a study of 40 cases treated with various techniques and followed for a period up to seven years. Twenty-five were under two years of age; 34 were below twenty. The location was as follows: eyelids, 14; lips, 4; nose, 4; face and neck, 16; scalp, 2; other parts of the body, 4. (In 4 cases the lesions were present on two different parts of the body.) In 7 cases the size of the tumor measured up to 4 cm. in diameter. One-fourth of all cases showed a considerable extension into soft tissues beneath the skin; three-fourths were purely superficial. Extremely large tumors are not found in our material. Almost all cases correspond to what is called "cavernous hemangioma" and "naevus vasculosus." The average time which elapsed between the last treatment and the last observation was seventeen and one-half months, the maximum being seven years.

TECHNIQUE

The treatments consisted in almost all cases in the application of radium. Only a few cases were treated by roentgen rays. In the latter, the radiation used was obtained with 200 kv. peak, 4 ma., filtered through 0.5 mm. Cu and 4 mm. celluloid at a distance of 50 cm. The technique of radium treatment was developed gradually; therefore the cases were treated in different ways and cannot well be compared. Radium element was used in the form of platinum needles, the thickness of the wall being 0.28 mm. Radium emanation was applied in the form of steel needles. The distance varied between 0 and 1 cm. In some cases no filter was used; in others, brass, lead, or silver. Experience showed that an erythema can be obtained approximately in the following manner:

Steel needles in contact without filter	3.5 to 5 mc-hr.
Steel needles at 1 cm. distance and 1.5 mm. brass filter	500 to 700 mc-hr.
Platinum needles in contact	20 mg-hr.
Platinum needles at 1 cm. distance	500 mg-hr.

The following technique was used several times: Platinum needles at 2 mm. distance, 30 to 50 mg-hr., or at 5 mm. distance, 50 to 60 mg-hr.

As a standard treatment within the last years, steel needles at 1 cm. distance with 1.5 mm. brass filter, dose of 250 to 300 mc-hr. at repeated intervals of six to eight weeks was used.

RESULTS

Before discussing the results obtained by therapy, the question arises as to how these tumors behave if left untreated. It may be said in general that the tumors we see in babies or in early childhood have been noticed a short time after birth and usually show a definite tendency to grow. In other cases the tumor remained constant for years and showed no spontaneous tendency to change. One case was a remarkable exception:

Anita E., aged eleven months, No. 10692; three hemangiomas were present; one on the forehead, 1.5 cm., another on the neck, 1 cm., both elevated; a third on the back, 2×3 mm., flat. The former two were treated repeatedly within one year using 40 to 50 mg-hr. in platinum needles at a distance of 5 mm. through 0.5 mm. brass filter. Examination after seven

* From the Roentgenological Department of the Massachusetts General Hospital, Boston, Mass.
† Rockefeller Fellow.

years showed an excellent result. The areas were hardly noticeable, but the non-treated area on the back had markedly faded out also.

Grouping the cases according to late results, we have obtained the following: An excellent result was obtained in 11 cases. This means that the previous tumor had disappeared entirely, and that the skin was normal. A very good result was seen in 20 cases. This should be interpreted as practical disappearance of the tumor with slight skin changes; this is, atrophy, induration, discoloration, or depigmentation. The group classified as improved includes cases in which the tumor was still present but smaller and bleached. No results were obtained in 5 cases. In the latter two groups it was necessary to determine whether the treatment had been insufficient, or whether the cases had not been followed long enough after completing the treatment. It happened in this group that only 2 cases were sufficiently treated or had been followed for a sufficient length of time.

Alice C. (No. 8482) had a pea-sized hemangioma on the scalp which was treated with 20 mg-hr. in platinum needles in contact, also, three applications of 150 mc-hr. each in steel needles at 5 mm. distance through 1 mm. brass filter; this treatment was given in a period of six months.

Mary C. (No. 8691), aged fourteen, presented a hemangioma affecting the whole lower eyelid including the conjuctiva; she was treated for a period of eight months, being given five applications of 40 to 80 mg-hr. in platinum needles at a distance of 0.5 cm.

Many cases do not show improvement for several weeks or months after treatment. It is our experience that a period of at least six months should elapse before passing judgment.

In 10 deep-seated tumors the results in general were very good. Two cases in this group had been insufficiently treated or had not been followed; 5 cases showed a very good or excellent result, and 3 cases improvement. One case gave a negative result, but might be considered as having had too small a dose:

Lester D. (No. 5818), aged six, had a hemangioma of the right eyelid which had been treated in another clinic with radium plaques followed by severe reaction, but without success. He was treated twice at this Hospital within four months, 85 mc-hr. and 100 mc-hr. in steel needles being used respectively, both at 1 cm. distance, and filtered through 2 mm. lead. As lead filters twice as much as brass only a small fraction of our standard dose was applied.

The following are cases from a group of 10 successfully treated tumors:

Margaret M. (9103), aged fourteen, with a hemangioma extending from the outer side of the cheek into the mouth, 3×3 cm. in size; within twelve months she received three 300 mc-hr. standard treatments outside, and one 220 mc-hr. treatment inside. Within the course of a year the lesion had disappeared entirely.

Patrica B. (19198), aged five, had a hemangioma affecting the left upper eyelid, displacing the eyeball; she received 240 mc-hr. standard treatment and two roentgen treatments of two-thirds of an erythema dose within two and one-half months. The lesion healed almost completely within fifteen months, there remaining only a slight ptosis and some whitish tissue at the inner canthus.

Harold B. (5835), aged fourteen, presented an egg-sized hemangioma of the right cheek. He received within twenty months eleven treatments of 35 to 75 mg-hr. (radium element) in steel needles at different distances through 1 mm. silver filter—the lesion was reduced to a flat, small atrophic area, measuring 1×1.5 cm. The flat, but larger sized tumors also gave very good results.

METHOD OF TREATMENT

The question arises as to the importance of the methods of therapy—roentgen rays, radium, dose, filter and repetition of treatment.

Roentgen treatment was tried in one case without success:

Josephine B. (8585), aged eighteen, had a hemangioma of the leg 6 cm. in length, she was given two treatments of two-thirds of an erythema dose within four months. Two months later no change was observed, but this interval was rather short.

TABLE I

RESULTS IN DEEP-SEATED TUMORS

Case No.	Age	Type of Radium Treatment	Location	Dose Expressed Approximately in Erythemas	Observation Time	Results	Remarks
5835	14 yr.	(1) Steel needles (Ra element) 2 mm. distance 1 mm. silver filter 2×50 mg-hr., 75 mg-hr.	Cheek	?	6 mo.	Very good	Treatment through 20 months
		(2) 1 cm. distance 1 mm. lead 75 mg-hr.		1/10			
		(3) contact 1 mm. silver filter 7×50 mg-hr.		7×¾(?)			
5818	6 yr.	(1) 3×plaque		?	1 yr.	None	(1) Applied at another clinic
		(2) Platinum needles 1 cm. distance 2 mm. lead filter 90 mg-hr.	Eyelid	⅛–1/10			(2) (3) Dose very small
		(3) Steel needles 1 cm. distance 1.5 mm. lead filter 85, 100 mc-hr.		2×1/10			
10615	10 mo.	Steel needles 1 cm. distance 1.5 mm. brass filter 2×250 mc-hr.	Eyelid	2×½	7 mo.	Very good	
8193	3½ yr.	(1) Platinum needles 3 mm. distance 1 mm. brass filter 2×40 mg-hr.		?	7 mo.	Good	Very probably improved afterwards
		(2) Steel needles 1 cm. distance 1.5 mm. brass filter 2×200 mc-hr., 300 mc-hr.	Nose	2×⅔+⅔			
8905	19 mo.	Steel needles 1 cm. distance 1.5 mm. brass filter 2×300 mc-hr.	Nose	2×⅔	2 yr.	Excellent	
8691	14 yr.	Platinum needles 0.5 cm. distance	Eyelid		3 yr.	Some im-	Tumor affecting the whole eyelid in-

(TABLE I Continued)

Case No.	Age	Type of Radium Treatment	Location	Dose Expressed Approximately in Erythemas	Observation Time	Results	Remarks
		2×40 mg-hr. 50 60 mg-hr. 80		$\frac{2}{3}$ <1 >1		prove- ment	cluding conjunc- tiva
10053	4 mo.	Steel needles 1 cm. distance 1.5 mm. brass filter 6×250–280 mc-hr.	Eyelid	$6\times\frac{1}{2}$	Some weeks	Good	Very short observation time
9043	14 yr.	Steel needles 1 cm. distance 1.5 mm. brass filter 3×300 mc-hr. outside 220 mc-hr. inside	Cheek	$3\times\frac{3}{5}$ $3\times\frac{2}{5}$	2 yr.	Very good	
10198	5 yr.	Steel needles 1 cm. distance 1.5 brass filter 240 mc-hr. X-ray treatment $2\times\frac{2}{3}$ S.E.D.	Eyelid	$\frac{1}{2}$ $2\times\frac{2}{3}$	50 mo.	Excel- lent	
10656	baby	(1) Platinum needles 2 mm. distance 30 mg-hr. (2) Steel needles 1 cm. distance 1.5 mm. brass filter 190, 250 mc-hr.	Nose	? $\frac{2}{5}+\frac{1}{2}$	Some weeks	Some im- prove- ment	Observation time very short

Two cases showed a definite result:

James G. (8203), aged sixteen, had a hemangioma of the right cheek, 4 cm. in size; he received 200 and 300 mc-hr. standard treatment; this gave no result within one month. Administration of two-thirds of an erythema dose of roentgen rays reduced the tumor to two-thirds of its size within six weeks; during the two years that he was under observation marked improvement was noted. Patricia B. (10198), aged five (previously cited), presented a hemangioma of the entire left upper eyelid with displacement of the eyeball. She was first given roentgen treatment, two-thirds of an erythema dose, followed by marked improvement within about five weeks. After two further administrations of 240 mc-hr. standard treatment, the tumor showed only slight improvement. Roentgen treatment was repeated, the same dosage being given, which resulted in a progressing diminution, at least, for fifteen months.

In these 2 cases roentgen therapy was apparently more efficacious than radium; however, the delayed action of radium should be considered.

Undoubtedly it is possible to obtain good results with a relatively small dose applied only once. The following cases will illustrate this fact:

Wilfred H. (8998), aged eight—hemangioma of the ear extending into the canal; he received 250 mc-hr., standard treatment. Within the next fifteen months the lesion became flatter and smaller.

Evelyn M. (10510), aged thirty-four, complained of a small nevus of the nail of the fourth finger, measuring 3×5 mm.; she received 300 mc-hr., standard treatment; seven months later she was completely cured.

In some cases repeated treatments are necessary. We have used as high as six standard treatments within one year.

The amount of dosage is of great importance as shown by the following cases:

William R. (8394), aged nine months, had a hemangioma of the right upper lid, 1.5 cm. in size; he was given three applications of 20 mg-hr. each in platinum needles at 2 mm. distance through 0.5 mm. brass filter, but received very little benefit. He was then given 10 mg-hr. platinum needles, in contact without filter, thus increasing the dose; this was followed by reddening and scaling; seven months later there was only a wheat-sized thickening present, and the skin was of normal color.

Natalie M. (7207), aged three months, had a hemangioma of the right upper lip extending from the midline to the angle of the mouth. She first received a treatment of 15 mg-hr., then two treatments of 30 mg-hr. each, using platinum needles, at 1 mm. distance through 0.5 mm. brass filter; the tumor bleached out, but its size remained unchanged. After the administration of 290 mc-hr., standard treatment, the tumor became smaller so that the edge of the lip could be seen through the tumor. Seven months later, after administration of three additional standard treatments of 200 mc-hr. and 300 mc-hr. each, the tumor was reduced to a third of its former size and twelve months later was only faintly visible.

With contact treatment very good results in some tumors are obtained, as the following case illustrates.

Julia L. (10157), aged four months, presented a hemangioma of the upper eyelid, 1.25 cm. in size; she received two treatments with steel needles in contact, 5.5 mc-hr. and 3 mc-hr. respectively within ten months. Seven months later the lesion was hardly noticeable. Following the application of 5.5 mc-hr. the eyelashes showed transient epilation.

Table II

Results in Cases Treated Only with Standard Treatment (250–300 mc-hr., one application)

Case No.	Age	No. of Treatments	Total Dose in Erythemas	Observation Time	Results	Remarks
9432	6 mo.	1	⅔	3 yr. 3 mo.	Good	Dose apparently not sufficient for complete cure
8905	18 mo.	2	6/5	2 yr.	Excellent	
10241	6 wk.	4	2	6 mo.	Very good	
10308	35 yr.	5	3½	—	Improvement	Received up to 400 mc-hr.; not followed up
9998	8 mo.	1	½	15 mo.	Good	Continually improving
10053	9 mo.	6	3	Some weeks	Good	
9043	14 yr.	3+1	2+1½	2 yr.	Very good	Cheek inside and outside
10508	8 mo.	3	1½	3 mo.	Good	Short observation time
10524	6 mo.	3	1½	2 mo.	Good	Short observation time
8159	6 mo.	2	1½	4 yr. 4 mo.	Very good	
10510	34 yr.	1	½	7 mo.	Excellent	

The interval between treatment and the appearance of a change in the lesion varies from several weeks to several months; the best result was shown in the following cases:

Francis S. (7362), aged nine, had a hemangioma of the lower lip, 1.5 cm. in size; 40 mg-hr. in platinum needles was used at 4 mm. distance through 0.5 mm. brass filter. Twelve days later the lesion broke down and three weeks following treatment it had practically disappeared. In the previously cited case, Patricia B. (L0198), five weeks after administration of two-thirds of an erythema dose of roentgen rays the tumor was so reduced that the eyeball displacement had practically dis-

TABLE III

UNSATISFACTORY RESULTS FROM IRRADIATION

Case No.	Age	Type of Radium Treatment	Dose Expressed Approximately in Erythemas	Remarks
8482	49 yr.	Platinum needles, Contact, 20 mg-hr. / Steel needles, 0.5 cm. distance, 1 mm. brass filter, 3×150 mc-hr. — within 6 mo.	1 / $3\times1-1\frac{1}{2}$	After second treatment on the scalp, local permanent epilation resulted.
8691	14 yr.	Platinum needles, 0.5 cm. distance, 2×40 mg-hr. — within 8 mo.	$\frac{2}{3}$	After the last treatment over the eyelid (80 mg-hr.) erythema and desquamation resulted; later skin atrophy.
		50 mg-hr. — within 8 mo.	<1	
		60 mg-hr. — within 8 mo.	>1	
		80 mg-hr. — within 8 mo.		
10241	6 wk.	Steel needles, 1 cm. distance, 1.5 mm. brass filter, 4×210–290 mc-hr. — within 7 mo.	$4\times\frac{2}{3}-\frac{3}{5}$	Subsequent thinning of the eyebrows after repeated applications of ½ of an erythema dose.
10157	4 mo.	Steel needles, Contact, 2 mc-hr. — within 10 mo.	$\frac{2}{3}$	Transient epilation of eyelashes following second application of more than 1 erythema dose.
		$5\frac{1}{2}$ mc-hr. — within 10 mo.	>1	
		3 mc-hr. — within 10 mo.	$\frac{3}{5}$	
10215	5 mo.	Platinum needles, Contact, 0.5 mm. brass filter, 15 mg-hr. — within 1½ mo.	$?\frac{1}{3}-\frac{1}{2}$	Permanent loss of eyelashes following one application of several erythema doses.
		Steel needles, Contact, 1.5 mm. brass filter, 112 mc-hr. — within 1½ mo.	several (3–5) S.E.D.	

appeared. In other cases the progress was rather slow. Harold B. (previously cited) had a small egg-sized tumor—following the tenth treatment, over a period of twenty months this was reduced to 1.5 cm. After one or several treatments it was quite commonly noted that the lesion showed improvement for a considerable period even though nothing further was done. Robert M. (8905), aged eighteen months, had a rather deep-seated hemangioma of the left naso-ophthalmic depression. He received two 300 mc-hr. standard treatments. Two months later the tumor was reduced to one-half its size and had faded out considerably. In the course of the next year and a half the tumor practically disappeared. Wilfred H.; Anita H., and Natalie M., showed the same results.

IMPORTANCE OF AGE

The results are definitely better in the younger patients. The group of 25 cases below two years of age showed excellent results in 18; five showed a marked improvement, although these were only followed for a period of three months (and from our experience we can state with certainty that they improved further in the course of time); one case showed only moderate improvement fifteen months

after having had a standard treatment of 250 mc-hr. which apparently was insufficient; another case in this group was not followed.

Comparing the above group with one ten years of age and older, which comprises 10 cases, we see that the chances for healing and improvement in the latter group are not so striking. This group shows an excellent or very good result in only 3 cases, 4 showed improvement, 2 were not followed long enough to allow a definite statement, and one showed no change—this case had only one roentgen treatment, probably insufficient.

THERAPEUTIC INJURY

This may be transient or lasting. A few of our cases showed a mild degree of skin atrophy, usually associated with slight pigmentation; 2 cases showed permanent epilation and here evidently the dose had been too large.

Sylvia K. (10125), five months of age, had a hemangioma of the left upper eyelid; she received 15 mg-hr., in platinum needles, in contact with 0.5 mm. brass filter, and 112 mc-hr. steel needles in contact through 1.5 mm. brass filter. Both treatments were given within one and one-half months. During the following months the hemangioma disappeared, but the eyelashes in the center of the lid showed permanent epilation.

Alice Ch., aged forty-nine (8482), had a pea-sized hemangioma of the scalp; 20 mg-hr. platinum needles in contact were used, then three applications of 150 mc-hr. each in steel needles at 0.5 cm. distance through 1 mm. brass filter. Following the second treatment permanent epilation took place in an area of approximately 3 cm. Julia L., a previously cited case showed a transient epilation of the eye-lashes. Here also the dose was above the erythema.

The appearance of telangiectasis was mentioned in some of the case records; however, re-examination showed no true telangiectasis, but an irregular fading and discoloration had taken place; a few of the former vascular channels persisted.

The disturbance in tissue growth with scar-like shrinking of the lips and eyelids should be considered, with other possible cosmetic injuries. This question cannot be answered from our group of cases of hemangiomas of the lips, as the average time of observation is much too short, being only seven months. In the group of hemangiomas of the eyelids, the observation period is longer—fourteen months being the average time, but this also is much too short.

Two cases only have been followed for more than three years—a baby and a fourteen year old child. In both cases none of these changes have been observed.

The question of irradiating ulcerative hemangiomas has been thoroughly discussed in the literature. In our series we had one case of this type:

Robert S. (10524), aged six months, who had an ulcerative hemangioma of the left humerus, 3 cm. in size. Following the administration of 250 mc-hr., standard treatment, the lesion cleared up with disappearance of the ulcer, and after two similar treatments which were given within a few months, the lesion became pale, flat and much smaller.

DISCUSSION

Good results may be obtained with any of the various techniques used in the treatment of superficial and small hemangiomas. Greater depth dosage is required in deep-seated tumors. The treatment which is now used at this Hospital has been very satisfactory. The β radiation is excluded by the filter; the distance guarantees a certain depth dosage, and the treatment time is short which is of value in the treatment of children.

The roentgen ray is not used in the treatment of these cases at the Radium Institute in Stockholm, but the results obtained from cases treated at the Massachusetts General Hospital show that the lesion can be greatly reduced in size within a short period of time with this form of radiation. Definite conclusions, however, can be drawn only after treating a series of cases with roentgen rays only.

The end-results will depend upon whether or not the proper dosage has been given (at

least two-thirds of an erythema dose in infants, correspondingly more for adults), and upon allowing sufficient time to elapse (at least several months) before conclusions are drawn. Radium treatment when repeated was used at intervals of four to ten weeks. It has been our experience that the observation periods should be extended for two reasons: first, in some cases the lesion is slow to respond, and second, once improvement starts it may continue over a considerable period of time. In treating these cases, Forssell gives 80 per cent of an erythema dose at one time, and has obtained very good results. It would be interesting to follow in the future a group of untreated hemangiomas in infants to be compared with a group of treated cases to determine the percentage of spontaneous disappearance of the lesion.

CONCLUSIONS

The results of treatment by irradiation in the cases studied was considered very satisfactory, especially so in infants. The smallest dose with which an improvement was noted was one-half of an erythema; superficial and smaller lesions respond to radium applied in any form. For general use a standard treatment was worked out and proved very effective; this consisted in the application of emanation in steel needles at a distance of 1 cm., filtered through 1.5 mm. brass, dose 250–300 mc-hr. corresponding to one-half of an erythema dose. In a majority of the cases one-half to two-thirds of an erythema dose was required; this was repeated at varying intervals. The elapsed time between treatments should be as long as possible—many cases do not show prompt improvement. Once improvement has started it may continue for a considerable period of time. Good results are sometimes obtained with roentgen treatment using two-thirds of an erythema dose at one sitting. Large and deep-seated tumors respond well to treatment. Ulcerated hemangiomas present no contraindications.

In the treatment of these cases the smallest dose which will bring about improvement should always be used because of the better cosmetic results. It is probably unwise ever to use the full erythema dose. At this time the question of whether tissue growth disturbance may be caused later cannot be definitely answered by our studies.

Thanks are due to Dr. George W. Holmes, chief of the Roentgen-Ray Department, without whose support it would have been impossible for me to give this study the necessary amount of time and work.

Vol. XXVII, No. 2

A CRITIQUE OF STEREOROENTGENOGRAPHY*

By HENRY C. SWEANY, M.D.
CHICAGO, ILLINOIS

IN A critical study of over five thousand consecutive pairs of stereoroentgenograms of the chest, it has been my observation that distortions frequently appear that prevent accurate interpretation. The most common one is the appearance of the lung outside of the bony framework of the chest. These conditions and their causes have been discussed before from this Institution[6] where experimental work was reported on hog lungs, as well as on those of human patients. The purpose of this brief report is to simplify that experimental work to include only mechanical devices, so that possibilities may be demonstrated without the added confusion of bronchial and vascular markings.

Although Thompson[7] first suggested stereoroentgenography in 1896, Davidson[2] in 1897 applied the Wheatstone stereoscope in viewing films, and suggested the distortion effects of motion of the subject between the two exposures. Without going into the vast number of improvements made since then, let us assume that a correct technique is used of a nature similar to that advocated by Kurtz and Bridge,[3] and that the readings are performed in the correct manner.

EXPERIMENTAL

It was attempted, therefore, to show, in a graphic way, the principles underlying stereoroentgenographic observation. Accordingly, four cardboard boxes were placed one above the other on a thin aluminum tray, and on each box was placed a lead pellet, offset, so that one would not be placed over another. These pellets (designated hereafter as "A" pellets) were in a line perpendicular to the plane of the tube shift. Pellet No. 1 was 6.8 cm.; No. 2, 13.8 cm.; No. 3, 16.5 cm.; and No. 4, 19.3 cm., respectively, above the film. Five wire loops were placed on the different levels with the pellets, and one on the film. Corresponding to each of the "A" pellets there were placed four other lead control pellets (designated hereafter as "B" pellets) on the tray just above the film.

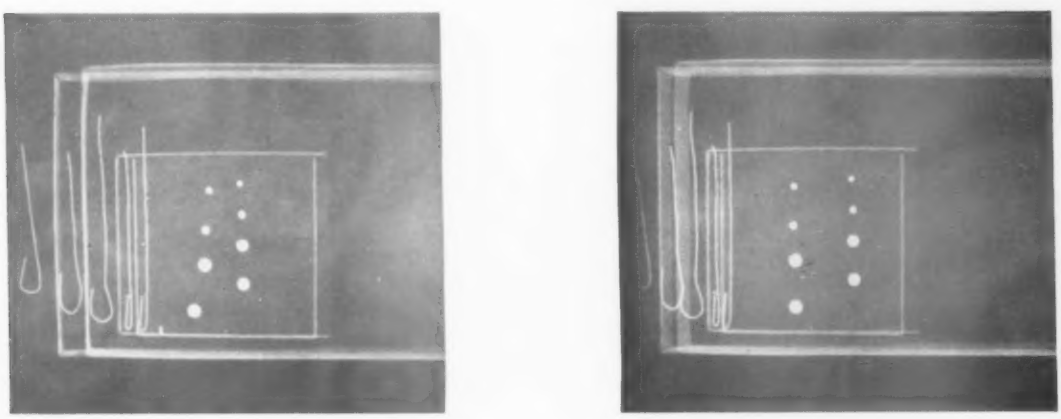


FIG. 1. A correct stereoscopic picture of pasteboard boxes with pellets and wire loops.

Five exposures were made; films No. 1 and No. 2 are a normal stereo (Fig. 1); in film No. 3 the pellets were moved a calculated distance along the line of, and with the tube shift, a distance equal to that caused by the shift, so that in the stereoscope all the pellets appeared on the same plane as the control pellets "B" (Fig. 2). As the tube shift was placed at 4 inches,

* From the Research Laboratories of the Municipal Tuberculosis Sanitarium, Chicago, Illinois.

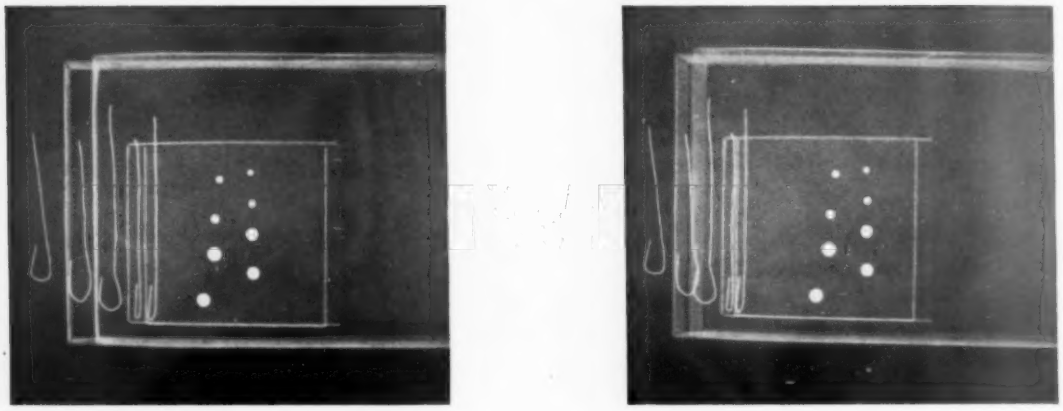


FIG. 2. An illusory picture of the same. The left row of pellets has been moved a distance calculated to equal the displacement from one film to the other produced by the tube shift. The result: loss of third dimension.

with a 40 inch distance, this movement was just 1/10 the elevation above the plate, i.e., 6.7 mm., for pellets No. 1, and proportional for 2, 3, and 4. The chief difference between the two groups was that the "B" pellets appeared sharp in outline, because they were so close to the film that the "penumbra" formed from the target was insignificant. As the experimental work was not done with a "line focus" tube, this fuzzy margin on the more distant pellets was quite marked.

In film No. 4, the pellets were moved double the distance of their position in film No. 3 (Fig. 3), and in film No. 5, they were moved the same distance as the No. 3 position was from No. 1 position, *only in the opposite direction* or opposite to the tube shift.

When these different pairs are viewed in the stereoscope, several effects are produced. The first pair of plates reveal the pellets in their normal relations; one pellet and a wire control appear on each box, with a control pellet opposite but on the plane of the film. Film No. 3, when substituted for film No. 2, reveals that the "A" pellets all appear in approximately the same plane as the "B" pellet controls, notwithstanding the fact that they are exactly the same distance away as in the No. 2 film (see Fig. 2). The looped wires, however, still appear on the boxes. When film No. 4 is substituted for film No. 3 (Fig. 3),

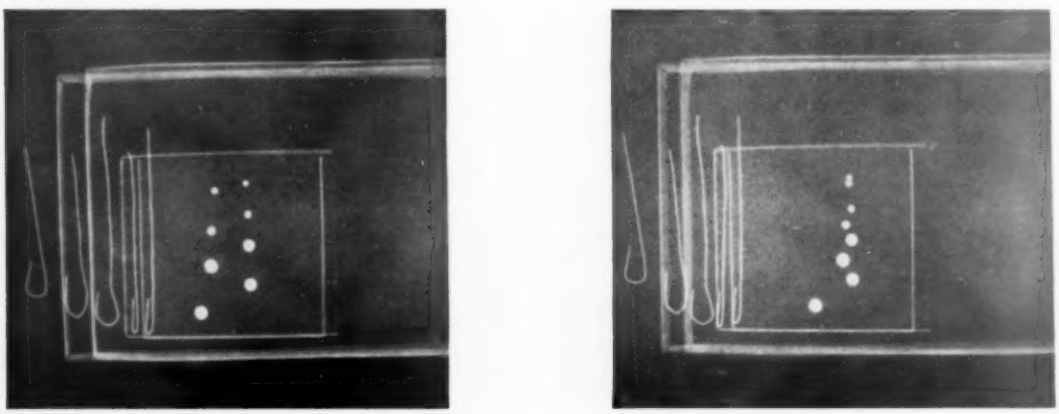


FIG. 3. Same as Figure 2 except a movement twice as great. Result: projection of "A" pellets beyond the film.

the position of the pellets appears beyond both the control wires and control pellets. In film No. 5, the movement has been opposite to the shift, consequently the objects appear nearer the observer than even the wire controls placed on the same box with them. It requires considerable convergent accommodation to fuse them, but when they do fuse into one object they are projected nearer the eyes than the wire controls.

In the course of this study, frequent reference was found to the unequal intensity of rays on different parts of the plate, causing some objects near the center to appear nearer than others of a corresponding density near the periphery. It has been suggested that this emphasis on the brightness will cause the object to appear nearer and out of its normal position. Wantz,[9] Stephenson,[5] and others, have emphasized this, while Victor's[8] viewing box is meant to correct false effects from improper illumination in reading films.

It is not our purpose to enter into a theoretical discussion of this problem, but a simple experiment was devised to test the principles in a practical way. A number of holes were bored in a pine board 1/4 inch thick, and lead disks were placed near the upper edge of the board in some holes, while others were left open. A stereoroentgenogram was made of this device and, contrary to our expectation, revealed all the objects in their true positions. The "white" lead disk shadows appeared to be a little nearer than the black open spaces, when looking with the direction of the rays, and a little farther away when the films were reversed, corresponding to their true positions on the upper edge of the quarter-inch board.

From a practical standpoint, therefore, the difference in position and relation of objects produced by differences in density are negligible. Only differences in clarity of vision appear to be affected. Although this by no means exhausts all the possibilities of different degrees of illumination, it points out clearly that gross distortion does not result from a difference in density. In fact, distortions resulting in the change of proportions may be caused by improper illumination or technique, but a "dislocation" or a change of relation of objects is only affected by motion between exposures.

DISCUSSION

Although stereoroentgenography may be standardized and rendered as accurate as many other optical sciences, it is apparent that it lacks, in general, the refinement of detail necessary for absolute measurements. The solution of the problem will no doubt be effected when a correct technique is used with absolute control of all movements between the exposures.

Many years ago Snook[4] attempted to standardize the technique and recommended a 2½ inch shift with a 25 inch tube distance, a 1:10 ratio. This arrangement reduces slightly the normal plasticity without straining the accommodating mechanism. It has given good results and as a consequence this ratio has been widely used.

Recently Kurtz and Bridge[3] have recommended a method based on sound physical principles. They point out that the average distance for comfortable vision is about 15 inches, and recommend this distance in viewing stereoroentgenograms. As the average interpupillary distance is 2½ inches, this forms a ratio of 1:6. On this basis they suggest a 45 inch distance, the nearest one that will completely show a large patient on a 14″×17″ roentgen film. The tube shift, therefore, must be 7½ inches to correspond. They insist upon a viewing distance similar to that of the target when the exposure is made. This is accomplished by using a pair of negative lenses to reduce the 45 inch distance to 15 inches. A larger or smaller ratio may be used and objects viewed with fairly normal accuracy, but with a ratio too large the depth would be abnormally great and the mechanism of accommodation would be strained, while a ratio too small would cause a loss of plasticity and would produce the effect of a flattened chest.

It should be emphasized also that of about eight different possibilities of viewing a stereoroentgenogram of the chest, there are only two correct ways, depending on whether the head is seen to the right or to the left. A general geometrical explanation was given by Clark[1] several years ago, while more recently Wilsey[10] has explained the practical aspects clearly in applying it to roentgenograms. He points out that the eyes should assume the respective positions of the target, when the exposures are made, and the right eye film should be the one that will permit the farthest view "around the right side" of the object, and left eye film should "see" around farther to the left.

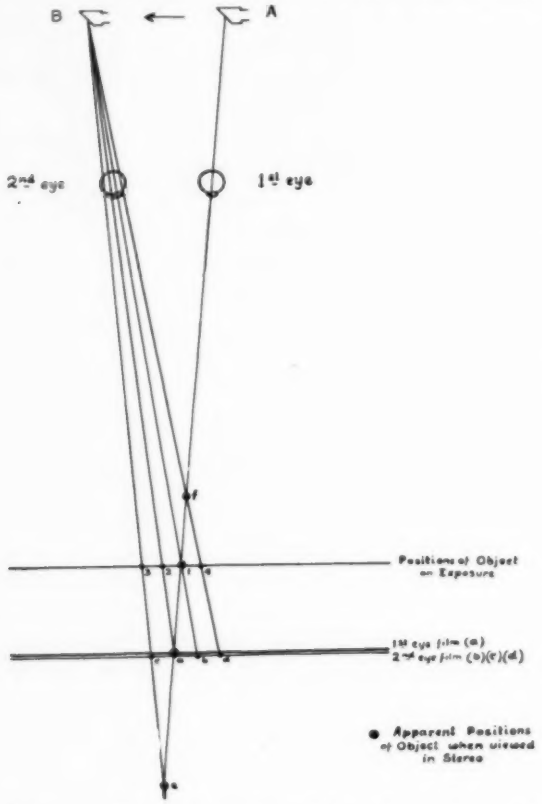


Chart 1. The first position of the tube at A records the object "1" on the first eye film at "a"; the second position of the tube at B records the image on the second eye film at "b." These respective images when viewed in a stereoscope are fused by convergent accommodation at the point "1" where the object was located when the exposure was made. Now if the object is moved to position "2" the tube shift is exactly neutralized and both images appear in the same position on the two films, so the fused images appear one at "a" in the same plane as the films. If the object is moved out to position "3" and another film exposed, the second eye film will show the image at "c," but fusion will take place out at "e" by a divergent accommodation, which causes the object to appear farther away. Now, if the movement is in the opposite direction or *against the shift* to position "4," the second eye film will show the image at "d." In order to fuse the images "a" and "d," it will be necessary to converge accommodation so that fusion will take place at "f." This convergence will give the sensation of an image at "f" on the near side of the object.

The problem of stereoscopic vision is principally one of experience and education. Helmholtz first explained it as a result of binocular vision. Each eye sees the object from a slightly different angle. The ability to localize an object in a stereoscope depends upon the degree of accommodation necessary to fuse the objects of each eye naturally as one object. Some can do it better than others, due to training or to a better visual sense. It depends upon the visual memory to retain the image in an imaginary position at the point of crossing of the paths of vision of the two eyes, where the two images are fused into one object. Each object, when properly seen in stereo, takes its respective place in the visual memory at this "fusion point" and will be near or far depending on the degree of convergent accommodation necessary to locate it. The ability to "see stereo" depends on this optical faculty.

Now, assuming that the ratio is nearly correct for comfortable vision, and an object has moved opposite to the tube shift (such as a raising of the diaphragm on exhalation), so that the apparent movement is greater than the most posterior part of the subject under observation, the accommodation will need to be greater to fuse the two images. As a result, the object will appear nearer the operator than the posterior ribs and entirely outside the chest.

Taking the other case where there is a movement *with* the shift, the accommodation is the opposite type or a *divergent* ac-

commodation. In such accommodation the rays reaching the eyes are more nearly parallel, and we usually associate it with more distant objects. When the movement is equal to, or less than the greatest total shift, there is gradual decrease of plasticity. When it is greater, the accommodation becomes still more divergent and the object becomes projected outside the chest wall or anteriorly if the films are exposed and viewed correctly. These various possibilities are outlined in Chart 1 and explained in the legend. Chart 1 reveals these various possibilities.

SUMMARY AND CONCLUSIONS

Simple experiments have been performed, attempting to show distortion effects produced in stereo-observation by (1) movement, and (2) difference in density of the objects. The effect of the former is real and pronounced; that of the latter is negligible for distortion effects, but considerable for the clarity of vision. While "distortion" effects may be produced by faulty technique or illumination, "*dislocation*" is produced only by motion between exposures.

Movement with the shift of the target at first reduces plasticity or depth until such movement equals that produced by the target shift, after which the image becomes projected away from the operator and in examinations of the chest will cause it to appear anterior to the breast plate. Movement opposite the target shift exaggerates the film shift so that in the viewing box the object will be projected towards the operator, requiring a greater convergent accommodation to locate it and, consequently, causing it to appear nearer the observer. In chest examinations it will sometimes give the appearance of being nearer than the posterior ribs and thus outside the chest cavity posteriorly.

REFERENCES

1. Clark, L. H. Theory and practice of stereoscopy. *Arch. Radiol. & Electroth.*, 1922, *26*, 317–323.
2. Davidson, Mackenzie. Quoted by Caldwell. Am. J. Roentgenol., 1918, *5*, 554.
3. Kurtz, H. F., and Bridge, Ezra. A method of precision in stereoscopic roentgenography. Am. J. Roentgenol. & Rad. Therapy, 1927, *18*, 370–377.
4. Snook, H. C. The practical use of the Wheatstone stereoscope. Am. J. Roentgenol., 1919, *6*, 39–47.
5. Stephenson, F. B. Shift measurements on stereoscopic plates; means of correcting false or doubtful visual impressions. *Radiology*, 1924, *2*, 326–329.
6. Sweany, H. C., Cook, C. E., and Kegerreis, Ray. A study of the position of primary cavities in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1931, *24*, 558–578.

   Sweany, H. C., Kegerreis, Ray, and Cook, C. E. On intrathoracic localizations by stereoroentgenography, with a consideration of some sources of error. *Radiology*. In press.
7. Thompson. *Med. News*, 1896, *68*, 268.
8. Victor. True vision stereoscope. *J. Radiol.*, 1922, *3*, 543.
9. Wantz, J. B. Principles of stereovision. *J. Radiol.*, 1923, *4*, 9–10.
10. Wilsey. *Radiology & Clin. Photography*, 1930, *6*, No. 4.

THE LIFE HISTORY OF A LITHOPEDION*

By L. R. SANTE, M.D., *and* FRED EMMERT, M.D.
ST. LOUIS, MISSOURI

A LITHOPEDION owes its origin to an unusual mode of termination of an extrauterine pregnancy. Ordinarily an ectopic tubular pregnancy results in the rupture of the tube or the extrusion of the fetus into the abdominal cavity during the early months of pregnancy. Occasionally the pregnancy may be primarily in the abdominal cavity. Under suitable circumstances the dead fetus lying free in the abdominal cavity may be tolerated by the individual for many years. Gradually calcium salts are deposited in the membranes about the fetus and a lithopedion is formed. The advent of the roentgen ray has made the diagnosis of lithopedion much more readily accomplished. The identification of fetal parts within the calcified shell is sufficient to establish the diagnosis. Many examples of lithopedions are present in the literature, but we have been unable to find any instance in the literature where the formation of a lithopedion was shown by roentgen examination from the stage of a full term pregnancy to the ultimate stage of calcification.

FIG. 1. (Courtesy of Dr. Zeller.) Shows full term abdominal pregnancy, September 5, 1923. After a short period labor pains ceased and patient continued in good health without expulsion of the fetus.

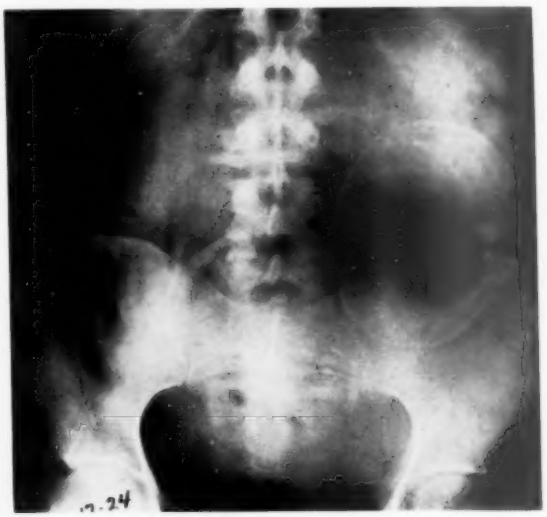


FIG. 2. (Courtesy of Dr. Zeller.) Examination four months later, January 17, 1924, shows the fetus still demonstrable although it was well tolerated by the patient. There is some reduction in size. The fetus continued to decrease in size at subsequent examinations.

The courtesy of Dr. F. F. Zeller permits us to report this case, and we are indebted to him for the clinical data and first three roentgen examinations.

The patient, aged twenty-nine, at the end of her second pregnancy had slight pains at the expected date of delivery. These soon ceased however, and she waited a whole month before consulting Dr. Zeller. Roentgen examination made at that time by Dr. Zeller's order disclosed a large, full term fetus, lying transversely, with the head to the left (Fig. 1). This was eight years ago. Since the patient experienced no discomfort, she refused any intervention and nothing further was done at that time.

Six months later another roentgen examination was made at the request of Dr. Zeller; the head seemed smaller, but the position was un-

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22–25, 1931.

changed. The top of the abdominal mass which was supposed to be the fundus and had originally been at the costal margin, was now about two fingers' width lower (Fig. 2). In January, 1931 (eight years later) a hard palpable mass, just above the symphysis, was all that was left of the original tumor.

Roentgen examination made at this time disclosed a fairly round calcified mass, within

Fig. 3. Film taken eight years after the original examination. All that now remains is a calcified body scarcely larger than a fist.

which several long bones could be identified as the sole remnant of the fetus (Fig. 3). The patient feels no discomfort, menstruates regularly and enjoys perfect health. She has been warned of the danger of subsequent pregnancy.

These roentgen examinations permit us to reconstruct the evolution of the lithopedion. The entire process developed over a period of eight years. The most remarkable thing about the progressive development of this lithopedion is the shrinkage in size from a normal full term fetus to a calcified structure no larger than a fist. It had always been our opinion in the past that a lithopedion was formed by calcification of a small fetus which had died in the early months of pregnancy; that it can result from a full term pregnancy is proved by this case.

DISCUSSION

Dr. M. C. Sosman, Boston. We have had three cases, in only one of which the diagnosis has been confirmed. It did not demonstrate the remarkable decrease in size which Dr. Sante has shown us, but it is of clinical interest. The patient was a young girl of twenty-eight years admitted because of painful diarrhea, with blood in the stools but with no fever. A plain film of the abdomen and pelvis gave us a shadow of calcified material in the left lower quadrant and a more detailed examination demonstrated the fetal structures. A subsequent operation revealed a lithopedion which showed the placenta, the remains of the cranial bones in a triangular shape, and the ribs, spine and long bones. (Presented two slides.)

On questioning the patient we learned that six years ago she missed three periods and thought she was pregnant. Following an automobile accident, at which time she was hospitalized, her periods recurred and have been normal since.

The striking thing clinically about this patient is that following the removal of the lithopedion her diarrhea cleared up completely and has not recurred. There were adhesions between the sac and the sigmoid and the local irritation presumably disturbed the bowel or its intrinsic autonomic nervous mechanism accounting for the diarrhea.

Dr. G. E. Pfahler, Philadelphia. I would like to refer to a somewhat similar case which I have had the privilege of examining during the past year,—a patient referred for treatment of hyperthyroidism and giving a history of retained fetus for eight years. We made an examination and found the complete outline of the entire fetus, with all bones a little larger than the last film shown by Dr. Sante but no capsule showing. This has been there, according to her history, and according to records, during eight years, with no decomposition whatever. The patient has had the hyperthyroidism relieved by a few treatments by roentgen therapy and was to be operated upon about this time. (This patient had her basal metabolism reduced to plus 10, and on December 7, was operated upon by Dr. Heller of Pottsville, but the mass was found so completely embedded in the

broad ligament that it was impractical to remove it without danger to the patient's life, therefore, the operation was not completed. Patient is reported as doing well.)

DR. SANTE (closing). The films secured had deteriorated with age and were really of such poor quality that I don't think we could have made out overlapping of the cranial bones.

DR. MANGES: May I ask how you determined that it was an extrauterine pregnancy?

DR. SANTE: Vaginal examination at this time reveals the mass to be extrauterine. The uterus is easily palpable, it is normal in size and position and is clearly outlined; the lithopedion forms a separate mass which can be moved around within considerable limits under the fluoroscope.

We are presenting this case not because of its being one of lithopedion formation, nor on account of the length of time which it has been carried without symptoms by the patient. We have had a number of other lithopedions and I feel sure they are not uncommon. The interesting thing about this case is that it was possible to demonstrate by roentgenographic examination that a full term fetus could shrink down to an object no larger than one's fist in its ultimate calcified state. It seemed to us that this was a very remarkable thing.

I feel sure that most of us have viewed lithopedion formation as the mummification or calcification of a *small dead fetus that had been aborted from a tube in the early months of pregnancy, not as the contraction and calcification of a full term fetus*. That shrinkage from the size of a full term baby to a structure no larger than one's fist is possible, seemed to us rather remarkable.

Vol. XXVII, No. 2

ROENTGENOGRAPHIC VISUALIZATION OF THE LIVER AND SPLEEN IN THE HUMAN*

A PRELIMINARY REPORT

By CARLO J. TRIPOLI, M.D., EMMERICH HAAM, M.D., *and* E. BURTON LEHMAN, M.D.
NEW ORLEANS, LOUISIANA

THE reticulo-endothelial system, particularly the liver and spleen, has long presented the most perplexing and yet the most interesting problems to investigators.

Much of the data concerning the physiology and the pathologic-physiology of this system has been derived by indirect means of observation. The reason for this is that the available methods of investigation have not permitted of any direct means of visualization of the most important parts of this system and especially of the liver and spleen, organs to which many functions have been ascribed, and concerning the physiology and pathologic-physiology of which much conjecture and many theories have been advanced.

Keith and Briggs[1] proposed a method of visualizing certain parts of the reticulo-endothelial system in rabbits by means of intravenous injections of halogenated fixed oils, iodized preparations being their media of choice. More recently Radt[2] suggested for this purpose thorium dioxide similarly administered. He found it possible to prepare colloidal solutions of this substance possessing a high diffusion coefficient with a relatively low toxicity. Both of these methods, due to the opacity of the injected products to the roentgen rays, make possible roentgenographic visualization of certain structures concerned in the dispersion and ultimate excretion of these products.

Through the kindness of Dr. Radt, who has placed at our disposal through the Heyden Chemical Corporation a quantity of his specially prepared thorium dioxide called "thorotrast," we have been able to carry on extensive visualization experiments on the liver and spleen—experiments incidental to investigation of various phases of reticulo-endothelial activity. As we believe that our efforts have resulted in a

FIG. 1. Anteroposterior view. Normal human.

FIG. 2. Anteroposterior view, showing complete roentgenographic visualization of liver and spleen.

* From the Department of Pathology and Radiology, Louisiana State University Medical Center and Charity Hospital, New Orleans, La.

definite roentgenological visualization of the liver and spleen in the living human, we deem it desirable to present our results in this preliminary communication, and briefly to outline the method used, which we believe opens a vast and new field of approach to the study of the entire reticulo-endothelial system.

Convinced by proper experimentation of the non-toxicity* of Radt's colloidal solution of thorium dioxide in the human, Mrs. T. R., aged fifty-five, with a diagnosis of splenic tumor was selected for attempted visualization of the organ. Besides the probability of a splenic tumor, she was suffering from myocardial hypertrophy and decompensation, chronic nephritis with hypertension and senile dementia. She was given thorotrast intravenously in 25 c.c. doses. Three doses at two-day intervals were administered. Two days after the last injection, a plain anteroposterior roentgenogram was taken at a distance of 55 cm. with a Potter-Bucky diaphragm, using a potential of 78 kv., 30 ma., time, $4\frac{1}{2}$ seconds. The roentgenogram obtained (Fig. 2) shows that complete visualization of both liver and spleen was accomplished.

At no time were untoward symptoms in the patient observed. Despite the marked pathology she presented there has been no change in her condition that could be even remotely attributed to the injections. In fact, her clinical condition improved. This seems to demonstrate the non-toxicity of the injected thorium although a single case is insufficient to permit definite conclusions.

In addition to certain observations which we are recording on various phases of reticulo-endothelial activity by this method, we are carrying on experiments which we believe will eventuate in important and easily performed tests having for their purpose the evaluation of liver and splenic function.

* Stewart et al.[3] report that sometimes very severe reactions result from the injections of the thorium dioxide solution. We have, to date, 15 human cases fully injected and visualized roentgenographically by the above method. No immediate or late untoward results in either animal or human have been encountered as yet. However, our series is too small for any definite conclusions and the warning of the above authors should be heeded and further investigations of possible dangers conducted.

REFERENCES

1. KEITH, W. S., and BRIGGS, D. R. Roentgen ray visualization of spleen following injection of emulsions of halogenated oils. *Proc. Soc. Exper. Biol. & Med.*, 1930, *27*, 538–540.
2. RADT, P. Eine neue Methode zur röntgenologischen Sichtbarmachung von Leber und Milz durch Injektion eines Kontrastmittels (Hepato-Lienographie). *Med. Klin.*, 1930, *26*, 1888–1891.
3. STEWART, W. H., EINHORN, M., and ILLICK, H. E. Hepatography and lienography following the injection of thorium dioxide sol (Thorotrast). AM. J. ROENTGENOL. & RAD. THERAPY, Jan., 1932, *27*, 53–58.

UNUSUALLY LOCATED LIPOMA, COMPLICATED BY A FOREIGN BODY

By IMRE WEITZNER, M.D.

NEW YORK CITY

THE patient, aged sixty, who is a physician's father, has a family and personal history unimportant until his present illness, which dates back fourteen years.

About fourteen years ago, he started to complain of an annoying rheumatic pain in his left buttock region. His family doctor diagnosed the condition as a muscular rheumatism, and advised massage and prescribed internal medication. As his condition did not improve, he sought the advice of other physicians. The diagnoses differed, one was muscular rheumatism, one, sacroiliac arthritis and another sciatica. The treatment was conservative, as previously. The result—negative.

Three or four years passed with no better result, after which he tried orthopedic surgeons, who administered plaster bed and injections in the sacroiliac joint as well as in the sciatic nerve. As the patient saw no change in his condition, he abandoned visiting physicians

In September, 1928, he saw a tumor developing around his left hip joint. At the same time, the left sacroiliac region became more painful. Six months after, he visited three prominent orthopedic surgeons who advised roentgen examination.

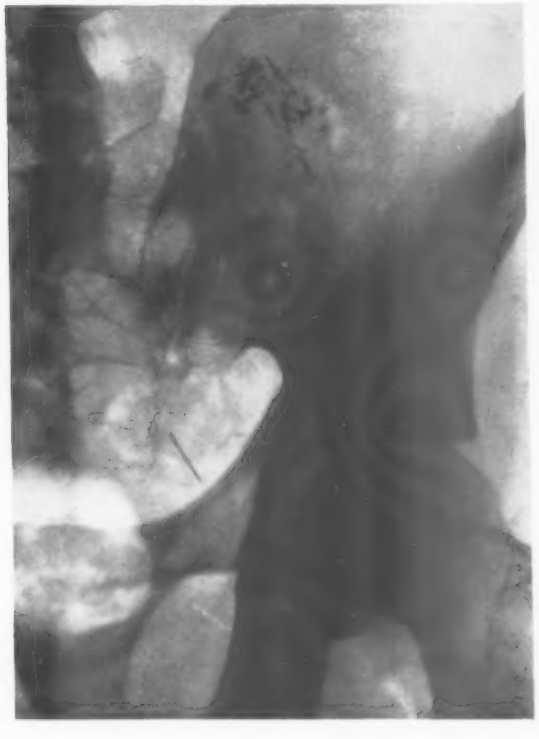


Fig. 1. Anteroposterior view. Lemon-sized circumscribed tumor is overlapped by the needle.

Fig. 2. Left lateral view. This shows the subgluteal tumor clearly. The needle is at the left about one inch from the tumor. The dense square shadow is a skin mark.

This was the first time I saw the patient. A roentgenogram taken in the anteroposterior view of the pelvis revealed no evidence of bone or joint pathology, except a slight structural difference of the upper end of the left femur, as compared with the right. The film also showed evidence of a needle and some opaque substance in the soft tissue (Fig. 1). My diagnosis was probable chondroma, originating from the rare-

fied area at the neck of the left femur. The origin of the needle and the opaque substance, as I learned later, and the presence of which was unknown to the patient, dated back twelve years to the time of the injections.

The opinions of the attending physicians differed concerning the nature of the tumor. They could not exclude, with absolute certainty, malignancy or malignant degeneration. The cause of the stitching pain of which the patient complained was thought to be the needle.

At the beginning of September, 1929, the pains became unbearable, and it was decided to operate and, if possible, remove the needle. I localized the needle. The roentgenogram taken in the left lateral view showed, in addition to the needle, which was very superficial, a well-circumscribed, encapsulated, lemon-sized shadow (Fig. 2) near the postinferior tuberositas, at the approximate region of the sciatic nerve. It was about one inch from the needle.

The operation was performed in September, 1929, by Dr. Meyer, surgeon of the Hospital for Joint Diseases. A large, semilunar incision was made, which extended from the greater trochanter to the spine. A large mass of tumor sprang to the surface which was under terrific pressure. The tumor had a peduncle, which at its end had a lemon-sized tumor, proved to be lipoma. With one incision, the needle was found and removed. The patient made an uneventful recovery with a complete absence of any pain.

This case is interesting because of the unusually located lipoma in the gluteal muscles, which originated from the lipoma located under the skin, around the hip; the lipoma under the muscles causing very probably, the constant pressure on the sciatic nerve, misleading the diagnosticians. The needle to which was attributed the stitching pain, proved to be harmless, on account of its superficial location.

Vol. XXVII, No. 2

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Editor: Lawrence Reynolds, M.D.

Editorial Board: A. C. Christie, M.D. E. H. Skinner, M.D. L. S. Taylor, PH.D.

Advisory Board for Pathology: James Ewing, M.D. Eugene Opie, M.D.

Collaborating Editors: The Officers and Committee Members of the Societies of which this Journal is the official organ, whose names appear on this page, are considered collaborating editors of this Journal.

Foreign Collaborators: A. Béclère, M.D., Paris, Gösta Forssell, M.D., Stockholm, G. F. Haenisch, M.D., Hamburg, R. Ledoux-Lebard, M.D., Paris.

Publisher: Charles C Thomas, 220 East Monroe St., Springfield, Ill.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich. Office of publication, 220 E. Monroe St., Springfield, Ill. Information of interest to all readers will be found on page iv.

Officers and Standing Committee

THE AMERICAN ROENTGEN RAY SOCIETY

President: Leopold Jaches, New York City; *President-Elect:* William A. Evans, Detroit, Mich., *1st Vice-President:* B. R. Kirklin, Rochester, Minn., *2d Vice-President:* Ross Golden, New York City; *Secretary:* E. P. Pendergrass, University Hospital, Philadelphia, Pa.; *Treasurer:* E. L. Jenkinson, St. Luke's Hospital, Chicago, Ill.; *Historian:* E. H. Skinner, Kansas City, Mo.

Executive Council: F. M. Hodges, Chairman, 1000 W. Franklin St., Richmond, Va., C. A. Waters, Baltimore, Md., M. C. Sosman, Boston, Mass., L. Jaches, New York City, W. A. Evans, Detroit, Mich., L. Reynolds, Detroit, Mich., E. P. Pendergrass, Philadelphia, Pa., E. L. Jenkinson, Chicago, Ill.,

Committee on Laws and Public Policy: B. R. Kirklin, Chairman, Rochester, Minn., F. M. Hodges, Richmond, Va., W. E. Chamberlain, Philadelphia, Pa.

Committee on Safety and Standards: H. K. Pancoast, Philadelphia, Pa., W. D. Coolidge, Schenectady, N. Y., A. U. Desjardins, Rochester, Minn., H. J. Ullmann, Santa Barbara, Calif., B. H. Nichols, Cleveland, Ohio, G. E. Richards, Toronto, Canada, R. R. Newell, San Francisco, Calif.

Publication Committee: William A. Evans, Chairman, Detroit, Mich., F. M. Hodges, Richmond, Va., E. L. Jenkinson, Chicago, Ill.

Tube Committee: David R. Bowen, Chairman, Philadelphia, Pa., I. H. Lockwood, Kansas City, Mo., E. C. Ernst, St. Louis, Mo., G. W. Grier, Pittsburgh, Pa., E. A. Pohle, Madison, Wis.

Finance Committee: G. W. Grier, Chairman, Jenkins Arcade, Pittsburgh, Pa., T. A. Groover, Washington, D. C., J. W. Pierson, Baltimore, Md.

Committee for American Congress of Radiology, Chicago, 1933: E. L. Jenkinson, Chairman, Chicago, Ill., Lawrence Reynolds, Detroit, Mich., J. T. Murphy, Toledo, Ohio.

Member, National Research Council: W. F. Manges, Philadelphia, Pa.

Editor: Lawrence Reynolds, 110 Professional Building, Detroit, Mich.

Editorial Board: A. C. Christie, E. H. Skinner, L. S. Taylor.

Advisory Board for Pathology: James Ewing, Eugene Opie.

Thirty-third Annual Meeting: Detroit, Mich., 1932.

THE AMERICAN RADIUM SOCIETY

President: Sanford Withers, 304 Republic Bldg., Denver, Colo.; *President-Elect:* Burton J. Lee, New York City; *First Vice-President:* Edward H. Skinner, Kansas City, Mo.; *Second Vice-President:* G. W. Grier, Pittsburgh, Pa.; *Secretary:* William H. Cameron, 511 Fifth Avenue, New York City; *Treasurer:* Zoe A. Johnston, Jenkins Arcade, Pittsburgh, Pa.

Executive Committee: E. C. Ernst, Chairman, St. Louis, Mo., H. H. Bowing, Rochester, Minn., H. J. Ullmann, Santa Barbara, Calif.

Program Committee: B. J. Lee, Chairman, Memorial Hospital, New York City, E. H. Skinner, Kansas City, Mo., F. E. Simpson, Chicago, Ill.

Publication Committee: E. H. Skinner, Chairman, Kansas City, Mo., B. F. Schreiner, Buffalo, N. Y., Douglas Quick, New York City.

Research and Standardization Committee: G. Failla, Chairman, New York City, H. J. Ullmann, Santa Barbara, Calif., R. B. Greenough, Boston, Mass.

Education and Publicity Committee: G.E. Pfahler, Chairman, Philadelphia, Pa., C. L. Martin, Dallas, Texas, J. S. Ullman, Natchez, Miss.

Committee for American Congress of Radiology, Chicago, 1933: James T. Case, Chairman, Chicago, Ill., Albert Soiland, Los Angeles, Calif., Henry Schmitz, Chicago, Ill.

Seventeenth Annual Meeting: New Orleans, La., May 9–10, 1932.

Committee on Arrangements: E. C. Samuels, Chairman, 3503 Prytaria St., New Orleans, La., E. R. Bowie, L. J. Menville, L. J. Williams.

EDITORIALS

THE ROENTGEN TREATMENT OF AGRANULOCYTOSIS

THE recent paper of Gager and Speer[1] on the treatment of agranulocytosis with roentgen radiation confirms the evidence of Bucky and Guggenheimer, in 1922, and of Friedemann and others that bone marrow cells may be increased in number in the blood stream after proper irradiation. The same agency which is used to reduce the number of "granulocytes" in leucemia is also able, by a variation in the dosage to increase their production. Another possible clue as to the mechanism of action is seen in the harmful effects of roentgen-ray irradiation of patients with acute myeloblastic leucemia. There is some suggestion that some stages in the development of the polymorphonuclear leucocyte (myeloblasts) grow more rapidly when exposed to the roentgen ray, whereas other stages (myelocytes) stop growing, differentiate, become adult, and later die with senile changes or are eliminated from the body.[2] The possible good effects of the radiation treatment of agranulocytosis depend on the stimulation of myeloblasts to reproduce at a more rapid rate than the body processes have caused them to grow, thus increasing the number of cells which can mature into adult polymorphonuclear leucocytes. If the granulocytopenia is due to other causes than the failure of a sufficient number of myeloblasts to mature at the proper rate, little can be hoped for from this type of treatment. Care must be used in eliminating atypical forms of aleucemic leucemia, and lymphoblastoma, in which the bone marrow is reduced to a minimum, not because of failure to grow, but because of crowding out of the marrow tissue. One can "stimulate" the invading tissue to grow just as well as the normal myeloid cells, and thus make the process worse. In aplastic anemia, where all the elements of the bone marrow are reduced (red blood cells, platelets) the problem is quite different. The marrow shows but few of the primitive cells, instead of many primitive cells which are "dormant" and fail to mature.

For this reason, in the absence of a knowledge of the cell content of the bone marrow of a given patient, the roentgen treatment must be used cautiously, as it appears to be indicated for its effect on a specific stage of a special cell, and therefore cannot and should not be used routinely or indiscriminately on any patient with a diminution of elements in the peripheral blood.

RAPHAEL ISAACS

[1] Gager, L. T., and Speer, A. J. The roentgen treatment of agranulocytosis. Report of two cases with recovery. AM. J. ROENTGENOL. & RAD. THERAPY, Jan., 1932, *27*, 40–45.

[2] Isaacs, R. Blood changes in the leucemias and the lymphomata and their bearing on roentgen therapy. AM. J. ROENTGENOL. & RAD. THERAPY. 1930, *24*, 648–655.

LEONARD REU

1879-1931

DR. LEONARD REU of Buffalo, New York, died on November 2, 1931, after an illness of several months. Dr. Reu was born in Buffalo on January 13, 1879. After completing his public and high school education he attended Cornell University and subsequently the Medical School of the University of Buffalo from which he was graduated in 1904. He engaged in general practice until 1909, at which time he became roentgenologist to the Deaconness Hospital. He severed his connection with the hospital a year later, maintaining his private laboratory until a few months prior to his death.

Dr. Reu possessed a dynamic personality and was an energetic worker. His powers of observation were keen and he surpassed in technical and diagnostic ability.

Dr. Reu was elected treasurer of the American Roentgen Ray Society in 1913 at the Boston meeting and also the following year at Cleveland. He was a member of the New York State Medical Society, Erie County Medical Society, American Roentgen Ray Society and the Buffalo Radiological Society. He is survived by his wife and two children. His loss to the profession and community is most keenly felt.

LESTER LEVYN

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Thirty-third annual meeting: Detroit, Mich., 1932.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: New Orleans, La., 1932.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. G. W. Grier, Jenkins Arcade, Pittsburgh, Pa.
Annual meeting: New Orleans, La., May 9–13, 1932.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. I. S. Trostler, 812 Marshall Field Annex, Chicago, Ill.
Eighteenth annual session, 1932: To be announced.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. W. S. Lawrence, Medical Arts Bldg., Memphis, Tenn.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. J. J. Masterson, 401–76th St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N.Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. A Srauss, 518 Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Herpel, Good Samaritan Hospital, West Palm Beach, Fla.
Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Fauntleroy Flinn, 220 South Webster St., Decatur, Ill.
Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.
Next Meeting: Minneapolis, Minn., February, 1932.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

NEW YORK SOCIETY
Secretary, Dr. J. Bennett Edwards, Englewood Hospital Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. R. C. Hall, 258 Genesee St., Utica, N. Y.
Three meetings a year—January, May and November.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Reiley, Clearfield, Penna.
Next meeting, to be announced.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

ST. LOUIS ROENTGEN CLUB
Secretary-Treasurer, Dr. E. W. Spinzig, 316 Metropolitan Bldg.
Meets first week of each month. Time and place of meetings designated by president.

TEXAS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

UNIVERSITY OF MICHIGAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburgh, Va.
Next meeting, to be announced.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 p.m., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 p.m. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd-und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Nicolae Busila, 44 Elizabeta Blvd., Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

DR. JACHES HONORED

Dr. Leopold Jaches of New York, president of the American Roentgen Ray Society, has been appointed a member of the Subcommittee on Radiology of the International Hospital Association for the study of the care of patients in hospitals. This honor was conferred upon him by Dr. Hans Holfelder. The principal questions to be considered are the following:

1. Specialization of the entire field of roentgen diagnosis and radium therapy; its establishment as an independent specialty and its right to independent quarters in the hospital.

2. Centralization or decentralization.

3. Does the radiological division require its own bed units?

4. Arrangement and disposition of space and technical adjustment.

5. Scope and limitations of radium therapy in the hospital and conditions of its application.

Dr. Jaches is to represent the members from the United States. There are twelve countries in all, each sending one representative.

NEW OFFICERS

At a meeting of the Radiological Section of the Los Angeles County Medical Association held on December 16, 1931, the following officers were elected for 1932: President: Dr. W. E. Costolow; Vice-President: Dr. Karl Bonoff; Secretary: Dr. D. R. MacColl; Councillor: Dr. Kenneth Davis; Treasurer: Dr. Henry Snure.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Wilhelm Conrad Röntgen und die Geschichte der Röntgenstrahlen. By Dr. Otto Glasser, Cleveland Clinic Foundation. Mit einem Beitrag persönliches über W. C. Röntgen by Margret Boveri, Berlin. Paper, price, RM 27.00; bound, RM 29.60. Pp. 337, with 96 illustrations. Berlin: Julius Springer, 1931.

Notwithstanding that Roentgen belongs to the immediate past there has already sprung up a wealth of myth and legend about this remarkable discoverer. From the material of more than a thousand both popular and scientific articles Glasser has sifted the salient and ofttimes new facts of Roentgen's scientific life and has presented them in his book in a way that will fascinate not only those whose work lies in roentgenologic fields but also whoever has an interest in medical history. Very much to be welcomed is the reprinting of Roentgen's three papers about the new kind of rays he discovered and the reproduction of some of the earlier roentgenograms taken by Roentgen and by some of the pioneers. Both the scientific and popular reception of the discovery of the roentgen rays are adequately treated by excerpts from the scientific literature and the lay press. In the extremely interesting section written by Margret Boveri we are given a close insight into the personal side of Roentgen so that we come to know him intimately rather than as an abstruse master of experimental physics. Very pleasing also are the comments on the earliest days in roentgenology by European and American pioneers in brief memoirs written in letters to Glasser. One's enjoyment of the book multiplies with each re-reading. It is hoped that an edition in English will be immediately forthcoming.

E. T. Leddy

Second Annual Reports of the National Radium Trust and Radium Commission, 1930–1931. Price, 15¢, postage extra. Pp. 32. London, His Majesty's Stationary Office. May be purchased through the British Library of Information, 551 Fifth Avenue, New York City.

This booklet contains the annual reports (1) of the National Radium Trust and (2) of the Radium Commission of Great Britain for 1930–1931 as presented before Parliament. The first has three chapters: I, dealing with the changes in the membership of the Trust; II, giving a detailed account of the purchases of radium and a summary of the present position of radium and III, showing the audited accounts of the financial status of the Trust. The second includes the changes in the personnel of the Commission, a record of the sittings, a summary of the progress, development of policy of concentration, rental charges, progress at national centers, radium supply, national post-graduate school of radiotherapy, experiences with the four-gram bomb, care and custody of radium, the problem of radium officers and finally the question of clinical records and summary cards

The report states that the year has been largely occupied in developing the national radium centers and in preparing radium officers. The total amount of radium ordered or approved to be ordered by the Trust amounts now to 24.9 grams, of which 17 grams have been actually delivered to the centers. The plan was to concentrate the radium therapy at certain hospital centers, each of which had to be nominated by the medical faculty of the local university. Owing to the uneven geographical distribution of the universities, however, more recently the designation of certain hospitals without medical schools as radium centers is also being considered. The rental charge is 2 per cent per annum of the capital value of radium and containers loaned. So far four centers have been organized in Scotland (University of Aberdeen, Dundee, Edinburgh, and Glasgow), one in Wales (University of Cardiff) and eight in England (University of Birmingham, Bristol, Leeds, Liverpool, Manchester, Newcastle, Sheffield and Radium Institute of London, which is associated with Mount Vernon Hospital).

In connection with the Mount Vernon Hospital (Northwood) and the Radium Institute (London) three post-graduate courses have al-

ready been carried through. It has been arranged that some of the lectures in connection with the Cambridge Diploma in Medical Radiology and Electrology will be given at the School. The Radium Institute has also undertaken to produce national radon for the benefit of such national centers and other institutions as are prepared to observe certain conditions with regard to its use. No applications from individuals are considered. The uniform flat rate is one shilling per millicurie for the use of non-paying patients.

A four-gram bomb was allocated to the Westminster Hospital with the stipulation that only malignant diseases in three regions, i.e. breast, stomach and prostate, be treated for trial purposes. After a period of more than a year it was found—what has also been the experience abroad—that this form of radium therapy under the present conditions of knowledge cannot be recommended for treatment of cancer in the said regions. It was therefore felt by the Commission that the continued use of the four-gram bomb was not only uneconomical but unwarranted. During the coming year a more satisfactory distribution of this radium will be undertaken.

Great stress is laid on the clinical records and summary cards which were standardized by the Commission. Through an accurate follow-up it will be possible at the end of five years to draw some definite conclusions concerning the value of the radium therapy as applied in the centers.

T. LEUCUTIA

BOOKS RECEIVED

LEHRBUCH DER RÖNTGENDIAGNOSTIK. Von H. R. Schinz, W. Baensch and E. Friedl. Nebst Beitragen von M. Holzmann, A. Hotz, O. Jüngling, E. Liebmann, E. Looser, K. Ulrich. Band I and II. Third, enlarged edition. Price, paper M. 214; bound, M. 200. Pp. 1623, with 2714 illustrations in the text and 5 photographic plates. Leipzig: Georg Thieme, 1932.

A DOCTOR OF THE 1870's AND 80's. By William Allen Pusey, Sometime President of the American Medical Association and of the American Dermatological Association. Bound. Price, $3.00. Pp. 153, with illustrations. Springfield, Ill.: Charles C. Thomas, 1932.

A RADIOLOGICAL STUDY OF THE PARA-NASAL SINUSES AND MASTOIDS. By Amedee Granger, K.C.B., K.C.I., M.D., F.A.C.R., Professor of Radiology, Louisiana State University Medical Center; Director of the Department of Radiology, Louisiana State Charity Hospital, New Orleans. Cloth. Price, $5.50. Pp. 186, with 113 illustrations. Philadelphia: Lea and Febiger, 1932.

DIE RÖNTGENDIAGNOSTIK DER VERDAUUNGSKANALS, EINSCHLEISSLICH DER LEBER UND DER GALLENWEGE. Von Privatdozent Dr. H. U. Albrecht, Oberarzt an der medizinischen Universitätsklinik Frankfurt a. M. Mit einem Geleitwort von Professor F. Volhard. Paper, price M. 56; bound, M. 59. Pp. 493, with 828 illustrations. Leipzig: Georg Thieme, 1931.

SECOND ANNUAL REPORTS OF THE NATIONAL RADIUM TRUST AND RADIUM COMMISSION, 1930–1931. Price, 15¢, postage extra. Pp. 32. London, His Majesty's Stationery Office. May be purchased through the British Library of Information, 551 Fifth Avenue, New York City.

ELECTRICITE ET RADIOLOGIE MÉDICALES. Par Dr. Leon Gally, Radiologiste des hôpitaux de Paris, et Dr. Pierre Rousseau, Ancien interne des hôpitaux de Paris, Chef du laboratoire d'Electrologie a la Faculté de Médicine de Paris. Paper. Price, 10 fr 50. Pp. 220, with 56 illustrations. Paris: Librairie Armand Colin, 1931.

ATLAS DER RÖNTGENSTEREOSKOPIE. Von Dr. Max Cohn. I. Series, with 20 negatives and a stereoscope. Price, M. 22. Leipzig: Georg Thieme, 1931.

A NON-SURGICAL CONSIDERATION OF PROSTATIC ENLARGEMENT. Including a lecture on The Myth of the Bladder Neck Bar. By Edwin W. Hirsch, M.D., Associate in Urology, College of Medicine, University of Illinois; Urologist, Engelwood Hospital, Chicago, etc. Paper. Price, $2.00. Pp. 79, with illustrations. St. Paul, Minn.: Bruce Publishing Co., 1931.

GUIDE TO RADIOLOGIC DIAGNOSIS IN HEART DISEASE. Prepared with the aid of the Committee on Research of the Heart Committee by Geza Nemet, M.D. Paper. Price, 35¢. Pp. 25, with 31 illustrations. New York: New York Tuberculosis and Health Association, Inc., 386 Fourth Avenue, 1931.

CRITERIA FOR THE INTERPRETATION OF ELECTROCARDIOGRAMS. Prepared with the aid of the Committee on Research of the Heart Committee by Arthur C. DeGraff, M.D. Paper. Price, 35¢. Pp. 13, illustrated with electrocardiograms. New York: New York Tuberculosis and Health Association, Inc., 386 Fourth Avenue, 1931.

RÖNTGENOLOGISCHE BEOBACHTUNGEN ÜBER DIE BEWEGUNGEN DER WIRBELSÄULE. (*Acta radiol., Suppl. XIII.*) Von Sigvald N. Bakke, Stadtisches Krankenhaus "Haukeland," Bergen. Paper. Price, Swed. crowns 10.00. Pp. 75, with 24 illustrations. Stockholm: P. A. Norstedt & Söner, 1931.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Stuhl, L.: Anatomic and radiologic aspects of some meningiomas of the convexity of the brain . . . 279

Neck and Chest

Zimmern, A., and Arvanitakis, G.: The roentgenography of discrete lesions of the lung . 279
Dethmers, A.: Congenital cysts of the lungs . . 280
Saupe, Erich: The lung findings in lymphogranulomatosis . . . 280
Loben, Franz: New observations on the azygos lobe . . . 280
Hjelm, R.: Two cases of varices of the esophagus diagnosed by roentgen examination . . 280
Clerc, Haret and Frain: Tumor-like aspect of ectasia of the descending aorta . . . 281
Kirsch, Oskar: The orthodiagraphic evaluation of the heart in childhood . . . 281

Abdomen

Desjardins, A. U.: Roentgenologic exploration in cholecystitis and biliary lithiasis . . 281
Gräberger, Gösta: Roentgen diagnosis of internal biliary fistulas . . . 281
Surmont, J.: On a rare anomaly of the duodenum . . . 281
Gräberger, Gösta: Infected intraperitoneal hematoma diagnosed by roentgen examination . . . 282
Salotti, Adelchi: Roentgen study of the movements of the jejunum . . . 282
Bignami, G., and Agati, Dino: Sequels of perforation of a duodenal ulcer . . . 283

Gynecology and Obstetrics

Grunspan-de Brancas, Mathilde: Radiology in obstetrics . . . 283

Genitourinary System

Hunt, Verne C., and Mayo, Charles, 2nd: Actinomycosis of the kidney . . . 283
Graham, Allen: Pathology of renal tumors . . . 284
Nichols, B. H.: Tumors of the urinary tract . . 284
Heckenbach, W.: Roentgen findings in a case of clogged kidney . . . 285
Tourne, W., and Damm, E.: On the retention of uroselectan . . . 285

Nervous System

Bianchi, Giovanni: Clinical and roentgen study of two cases of Billroth's traumatic spurious meningocele . . . 286

Skeletal System

McLean, Stafford: I. The roentgenographic and pathologic aspects of congenital osseous syphilis . . . 286
McLean, Stafford: II. The correlation of the roentgenographic and pathologic aspects of congenital osseous syphilis . . . 288
McLean, Stafford: III. Correlation of the roentgenologic picture with the gross and the microscopic examination of pathologic material in congenital osseous syphilis . . . 290
McLean, Stafford: IV. The correlation of the clinical picture with the osseous lesions of congenital syphilis as shown by the x-rays . . . 290
Park, Edwards A., Jackson, Deborah, and Kajdi, Laslo: Shadows produced by lead in the x-ray picture of the growing skeleton . . . 290
Ledoux, E., and Cottet, P.: Multiple enchondromata associated with exostoses in an infant who had previous hypertrophy of the thymus . . . 291
Faulkner, D. M.: Tuberculosis and Köhler's disease . . . 291
Lapidus, Paul W.: Fracture of the metatarsal bones simulating thrombo-angiitis obliterans . . . 292
Miller, Oscar Lee: Plastic bone repair after therapeutic irradiation . . . 292
Freund, Ernst: On the question of deformity of the femoral head following closed reduction of congenital dislocation of the hip joint . . . 292
Piergrossi, Aldo: On a case of eburnizing monomelic ostosis (melorheostosis) . . . 293
D'Amato, Guiseppe: Some structures found in the spongiosa of the metaphyses of the long bones . . . 293
Blaine, Edward S.: Spondylitis traumatica tarda (Kummell's disease) . . . 293
Talia, Ferdinando: Painful hemisacralization of the sixth lumbar vertebra . . . 294
Codman, Ernest A., and Akerson, Irving B.: The pathology associated with rupture of the supraspinatus tendon . . . 294
Coley, William B.: Multiple myeloma . . . 295
Knoll, W., and Matthies, Th: Visualization of joints by means of iodipin filling . . . 295
Copeland, Murray M.: Bone metastases . . . 295

General

Aubertin, Charles: Recurrent leucocytosis in the blood of a radiologist . . . 296

KIRKLIN, B. R., and MORTON, S. A.: Roentgenologic changes in sarcoid and related lesions . . . 296
WARTHIN, ALDRED S.: The genetic neoplastic relationships of Hodgkin's disease, aleukaemic and leukaemic lymphoblastoma and mycosis fungoides . . . 296

ROENTGEN AND RADIUM THERAPY

KAPLAN, IRA I.: The emergency value of roentgen therapy in pediatrics . . . 297
REGAUD, CL.: Some peculiarities of the life of cancerous tissues as evidenced by radiotherapy . . . 298
GENDREAU, J. E.: Far-reaching effects of gamma rays and short x-rays upon the human heart . . . 298
GABRIEL, GERHARD: Indications and results of grenz-ray therapy . . . 298
FREUND, LEOPOLD: The present methods and results of radiation therapy of cancer using subdivided doses . . . 298
TREVES, NORMAN, and PACK, GEORGE T.: The development of cancer in burn scars . . . 299
NURNBERGER, L.: Roentgen mutations and late injuries from roentgen rays . . . 299
KLEINSCHMIDT, O.: The roentgen treatment of carcinoma . . . 299
TRAUTMANN, EDGAR, and PANSDORF, HANS: Roentgen treatment of chronic encephalitis . . . 300
HAYER, E.: Roentgen therapy of toxic goiter . . . 300
REGAUD, CL.: Rational fundamentals and indications of radiotherapy . . . 300
WOOD, FRANCIS C.: The palliative therapy of malignant growths . . . 301
LAZARUS-BARLOW, W. S.: Experimental use of a large quantity of radium in treatment . . . 301
PHEMISTER, DALLAS B.: Undifferentiated round-cell sarcoma . . . 301
LAMBRANZI, MARIO: On the roentgen therapy of a rhinopharyngeal fibroma . . . 301
DENIER: Treatment of hay fever by radiotherapy . . . 302
ZIMMERN, A., and BRUNET, R.: A new case of arthritic gangrene in a diabetic treated by irradiation of the suprarenal region . . . 302
DENIER: Cure of recurrent lymphangioma by radiotherapy of the spleen . . . 302

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Stuhl, L. Aspects anatomiques et radiologiques de quelques méningiomes de la convexité du cerveau. (Anatomic and radiologic aspects of some meningiomas of the convexity of the brain.) *Bull. et mém. Soc. de radiol. méd. de France*, April, 1931, *19*, 159.

In comparing the pathologic specimens of removed meningiomas with the roentgenograms taken previous to operation, the following characteristics were established: (1) meningiomas displace the cerebral substance without invading it, thus producing veritable niches; (2) they penetrate into crevices and extend on the surface of the bone provoking destruction and osteogenic reactions which appear in the form of erosions, voluminous hyperostoses or fine spicules; (3) they produce a hypervascularization adjacent to the tumor, leading to accentuation of the vascular imprints of the diploë, with considerable new formation of blood vessels, these latter penetrating into the adjacent bones where they produce veritable canals, and (4) they are subject to calcareous degeneration, the oldest parts of the tumor being affected first.

The preoperative diagnosis of meningiomas is important since they belong to that group of intracranial tumors which are curable by surgical intervention.—*T. Leucutia.*

NECK AND CHEST

Zimmern, A., and Arvanitakis, G. La radiographie des lésions discrètes du poumon. (The roentgenography of discrete lesions of the lung.) *J. de radiol. et d'électrol.*, Jan., 1931, *15*, 1–21.

I. The theoretical basis of pulmonary roentgenography. Excellent definition is one of the primordial requirements of roentgenographic films of the chest. The second desideratum consists in richness of detail, permitting the visualization of the fine vascular arborizations. The abundance of detail is best obtained by a perfection of the contrast.

1. Definition. To obtain good definition one must (*a*) observe certain elementary principles of geometric optics and (*b*) attempt complete immobility of the patient and his organs. For the first, the authors advise teleroentgenography at a distance of from 1 m. 20 cm. to 1 m. 50 cm. This increases the sharpness of the image, corrects the focal astigmatism, produces a homogenization in depth and intensity of the shadow, lengthens the shadow cone of very small foci so that they reach the film, and reduces to a minimum the deformity of the parts distant from the central ray leading to a nearly orthodiagraphic projection. For the second, very short exposures (from 1/30 to 1/100 of a second) are recommended.

2. Richness in detail. This consists in the ability to demonstrate very discrete modifications of the density of the pulmonary parenchyma. Since the visualization of fine structures depends on the absorption of roentgen rays, it follows that soft rays must be used with preeminence. A series of experiments carried out by the authors on this subject has shown that the application of hard roentgen rays results in considerable loss of detail with poor differentiation between the coarse and fine structures. It is understood, of course, that the films are correctly exposed and developed.

3. Contrast. Whereas the selection of the quality of the roentgen rays is essential to obtain good detail, there are certain procedures which help to still further increase the difference in the proportional density of the various structures, resulting in greater contrast. Such procedures are the use of double-coated films, intensifying screens and the elimination of scattered radiation. For this latter, the authors advise the reduction as much as possible of the high tension (lower tensions giving less secondary radiation), the use of Potter-Bucky diaphragms and the increase of the focus film distance. The increase of the object film distance, as advised especially by Groedel, failed in the author's experiments to produce any appreciable improvement in the contrast.

II. Critical considerations of the apparatus. In this part of the article, the type of tubes, electric generators, measurement of voltage, drop of voltage during operation, measurement of intensity, time of exposure, intensifying

screens and process of developing are discussed in detail.

III. Rational technique. The following technique is advised: the patient is placed with the chest against the film, the shoulders thrown forward and the exposure made in apnea at the moment of beginning inspiration. The time of exposure must be very short, from 1/100 to 2/100 of a second, the factors being: 5.5–6 Benoist (65 kv. max., disc rectification), 1 m. 20 cm. focus film distance, 200 ma. for 20 cm. chest thickness, 15 to 20 ma. being added for each additional centimeter, after correction of the resulting drop in the voltage. This should give a blackening intensity of 1.2 in the parasternal region, which, according to the authors' estimation, must be considered as the optimum density for good contrast.—*T. Leucutia.*

DETHMERS, A. Zur Kasuistik kongenitaler Kystenbildung in der Lunge. (Congenital cysts of the lungs.) *Acta radiol.*, Apr. 15, 1931, *12*, 135–139.

A woman of thirty-five was sent to the hospital with a diagnosis of tuberculosis of the lungs. Sagittal and frontal roentgenograms showed the whole right upper lobe filled with small circular shadows distributed irregularly; they were sharply circumscribed and enclosed air. One of the cavities showed a fluid level. The ring shadows were seen only in the right upper lobe. The other lobes, the heart, mediastinal organs and diaphragm were normal. It seemed probable from this picture that the right upper lobe of the lung was filled with congenital cysts and this diagnosis was confirmed by filling the cysts with lipiodol. The patient was kept under observation for awhile. Her temperature remained normal, the expectoration decreased and she was discharged in good condition.—*Audrey G. Morgan.*

SAUPE, ERICH. The lung findings in lymphogranulomatosis. *Klin. Wchnschr.*, 1930, *9*, 1495.

The author states that lymphogranulomatosis of the lungs is not so rare as we have believed. Held has recently published an extensive study of this subject (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1930, *41*, 191). He groups these cases as follows: (1) simple mediastinal lymph node involvement; (2) mediastinal tumors with direct involvement of the lungs; (3) independent processes of the lungs without connection with the mediastinal tumor; (4) disseminated types. The author has seen one case belonging to Group 4, and several patients of Groups 2 and 3. The histories of 10 cases are related and a number of roentgenograms show the lesions. He comes to the conclusion that it is not possible to make a definite roentgen diagnosis of lymphogranulomatosis of the lungs. This is particularly true for cases of hilum carcinoma with large mediastinal metastases. However, in such cases, the unilateral involvement speaks more for hilum carcinoma while a bilateral enlargement of the mediastinum points to Hodgkin's disease. Very difficult to diagnose is the disseminated type without enlargement of the mediastinum. It is also possible that an accompanying pleural exudate can cover the foci in the lungs and make recognition almost impossible. One must also remember the close relation between lymphogranulomatosis and tuberculosis. It has also been observed that an involvement of the lungs may be diagnostic both clinically and roentgenologically earlier than the involvement of the palpable lymph glands.—*E. A. Pohle.*

LOBEN, FRANZ. Neuere Beobachtungen über den Lobus venae azygos. (New observations on the azygos lobe.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1931, *43*, 231–236.

The author observed 2 cases of azygos lobe; in one the condition was associated with tuberculosis, the collapse therapy leading to no complications, and in the second it occurred in brother and sister, proving an occasional familial nature.—*T. Leucutia.*

HJELM, R. Zwei Fälle von Röntgendiagnostizierten Oesophagusvarizen. (Two cases of varices of the esophagus diagnosed by roentgen examination.) *Acta radiol.*, Apr. 15, 1931, *12*, 146–151.

In cases of hemorrhage from the digestive tract when roentgen examination of the stomach and duodenum gives negative results an examination should be made for varices of the esophagus, particularly in cases in which there are enlarged spleen and ascites. When a spoonful of contrast emulsion is given remnants of it will lodge in the hollows and grooves between the varices and they can be seen projecting into the lumen of the esophagus. If the varices are numerous and large the fissure-like lumen of the empty esophagus, visible after the pas-

sage of the contrast medium, will be broader than normal. The author describes 2 typical cases and illustrates them with roentgenograms. His pictures are very similar to those previously published by Wolf and Hellmer.—*Audrey G. Morgan.*

Clerc, Haret and Frain. Aspect tumoral de l'ectasie de l'aorte descendante. (Tumor-like aspect of ectasia of the descending aorta.) *Bull. et mém. Soc. de radiol. méd. de France*, April, 1931, *19*, 164–167.

Two unusual cases of aneurysm (in one associated with massive pleural effusion on the left side) are briefly described. In both instances a clinical diagnosis of pulmonary neoplasm was made, the true condition being found only at post mortem. The opinion is expressed that the roentgen diagnosis, especially in tumors of the left thorax, should not be considered entirely conclusive.—*T. Leutcutia.*

Kirsch, Oskar. The orthodiagraphic evaluation of the heart size in childhood. *Klin. Wchnschr.*, 1930, *9*, 1574.

The author made an extensive study of the heart size in childhood by the orthodiagraphic method. He concludes that it is not permissible to use the absolute or relative width of the heart alone for diagnostic purposes. One should always correlate it with the length of the heart, sometimes also with the sagittal diameter. The body length must also be considered in this connection.—*E. A. Pohle.*

ABDOMEN

Desjardins, A. U. L'exploration radiologique dans la cholécystite et la lithiase biliare. (Roentgenologic exploration in cholecystitis and biliary lithiasis.) *J. de radiol. et d'électrol.*, Feb., 1931, *15*, 65–83.

This article is a historical survey of the development of roentgenologic exploration of the gall-bladder and especially of gallstones. One may distinguish three periods: the first, that of direct roentgenography of biliary calculi, from 1896 to 1910; the second, that of indirect signs, from 1910 to 1924; and the third that of cholecystography, from 1924 to the present time. The most salient contributions during these three periods are analyzed from a critical standpoint and their importance in the development of gall-bladder investigation discussed. Whereas in the first period positive information was obtained in only 15 to 50 per cent, in the second period this figure was increased to 75 per cent and in the third, with the advent of intravenous cholecystography, fully 95 to 97 per cent of pathologic gall-bladder conditions are now correctly diagnosed.

In the latter part of the article the work of Graham, Cole and Copher leading to the introduction of cholecystography, the influence of fats on gall-bladder function, the various substances employed as opaque media, the technique of both intravenous and oral administration of the dye, the reactions produced thereby, the interpretation and diagnostic value of the cholecystographic findings, and finally the avantages and disadvantages of the method are discussed at length. The article includes a bibliography of 98 references.—*T. Leucutia.*

Gräberger, Gösta. Beitrag zur Röntgendiagnose innerer Gallenfisteln. (Roentgen diagnosis of internal biliary fistulas.) *Acta radiol.*, Apr. 15, 1931, *12*, 164–174.

It is possible to diagnose internal biliary fistulas from the presence of air or contrast medium or both in the bile tract. In most cases the diagnosis has been made from barium in the bile tract. The author reviews the literature of the subject and describes a case of his own in which there was gas in the intrahepatic bile ducts and barium contrast medium in the gall-bladder. The patient was a woman aged seventy who complained of pain in the abdomen and gas distention. On roentgen examination contrast medium could be seen passing from the bulb of the duodenum into the gall-bladder, showing that there was a fistula between these two organs. Some days later on making a gall-bladder examination with tetraiodophenolphthalein the gall-bladder did not fill but there was air in the intrahepatic bile ducts. When the patient lay on her right side the air passed out of the liver. There had been no symptoms of gall-bladder disease or biliary fistula. Generally internal biliary fistuals are a late complication of cholelithiasis and there is a history of symptoms of that disease.

The author briefly mentions two other cases of barium contrast in the bile ducts after cholecystoduodenostomy.—*Audrey G. Morgan.*

Surmont, J. Sur une anomalie rare du duodénum (accolement des 2e et 4e portions avec angle duodéno-jéjunal à droite de la colonne

lombaire). (On a rare anomaly of the duodenum (adhesion of the second and fourth portions with the duodeno-jejunal angle to the right of the lumbar column).) *Bull. et mém. Soc. de radiol méd. de France*, April, 1931, *19*, 159–161.

The above rare anomaly occurred in a woman thirty years of age who had complained for a long period of vague dyspeptic disorders. The interesting feature is that the duodeno-jejunal angle, which is considered as one of the few fixed points of the abdominal cavity, was displaced to the right. There was no other congenital anomaly associated with this unusual condition.—*T. Leucutia.*

GRÄBERGER, GÖSTA. Röntgendiagnostiziertes infiziertes intraperitoneales Hämatom. (Infected intraperitoneal hematoma diagnosed by roentgen examination.) *Acta radiol.*, Apr. 15, 1931, *12*, 152–156.

A man aged forty-seven was operated on for appendicitis. The next day he had subfebrile temperature, vomited and had pain in the abdomen. His abdomen was distended but not rigid. His blood count showed 7,600 leucocytes, 5,600 of them polynuclears. As his condition did not improve he was sent five days later for roentgen examination with a clinical diagnosis of ileus. The diaphragm was freely movable on both sides and there was no exudate in the pleural sinus. There was pronounced meteorism of the whole colon. In the right flank at the lateral wall of the abdomen there was a homogeneous shadow several centimeters broad which pushed the cecum and colon toward the midline. It passed above into the liver shadow without any visible boundary and extended down to a plane just below the anterior superior spines of the ilium. The parts of the cecum and ascending colon adjacent to it did not show any signs of inflammation. A diagnosis of intraperitoneal hematoma was made. There seemed to be no definite indication for operation so expectant treatment was given. Another examination four days later showed that the right side of the diaphragm lagged perceptibly and there was a slight exudate in the pleural sinus. There was still a condition of relative ileus. The homogeneous shadow in the right flank remained unchanged but the middle part of the subperitoneal fatty layer had disappeared entirely so that the shadow of the transversus muscle passed without any visible boundary into the homogeneous shadow. The leucocytes had risen to 20,500, of which 17,500 were polynuclears. Evidently infection of the hematoma had developed gradually. Operation was performed at once and the diagnosis confirmed. The patient was discharged well a week after the operation.—*Audrey G. Morgan.*

SALOTTI, ADELCHI. Studio radiologico dei movimenti dell' intestino tenue digiuno. (Roentgen study of the movements of the jejunum.) *Radiol. med.*, Apr., 1931, *18*, 421–433.

The author studied the movements of the jejunum in the human being under normal conditions, using an ordinary barium sulphate paste which does not alter the tonus or movements of the various parts of the digestive tract. It is very hard to get good roentgen pictures of the jejunum on account of the rapidity of its movements, the varying motility in different parts and the action of the digestive fluids in diluting the opaque medium. Therefore very rapid pictures have to be taken. The author took rapid seriograms with an exposure time of a twelfth of a second. A number of these are reproduced, showing the different kinds of movement and the different phases of intestinal peristalsis. He describes the minute changes in the folds of mucous membrane which he thinks are brought about by the muscularis mucosae. An appearance which he calls the arrow sign indicates the direction of the loop of jejunum. In it the negative pictures of the valvulae conniventes are arranged like the barbs of an arrow, pointing in the direction of the flow.

There are different forms of peristaltic transportation which he calls stair-step, rotatory and transportation through short distances of 1 or 2 centimeters. These alternate with mixing movements. The different phases of these movements are shown in the illustrations. He gives general figures for the number of seconds required for rhythmical contraction, transportation, expansion of the valves and the pendulum movement of the loop. On an average the mixing movements require 40–50 seconds and the transportation 3–4 seconds, so that a complete series of movements takes place in about a minute, but this is influenced by various factors, such as the amount and nature of the food and the tonus and contractility of the loop, depending on the individual constitution.—*Audrey G. Morgan.*

Bignami, G., and Agati, Dino. Sugli esiti di perforazione di ulcera duodenale. (Sequels of perforation of a duodenal ulcer.) *Radiol. med.*, May, 1931, *18*, 545–565.

A case is described in a man of fifty-four who for years had had rather intense pain coming on some time after meals. The nature and site of the pain suggested duodenal ulcer. Between the attacks of pain there were intervals during which he seemed to be in perfectly good health. Some years before he came for examination he began to have attacks of slight icterus. He began to have pain at meal time which might have been caused by adhesions between the bile tract and the duodenum due to old inflammation. The pain was not at all characteristic of gallstones and was not accompanied by the other symptoms of cholelithiasis. Recently he had begun to have chills and fever, vomiting and pain in the liver. There was slight pain on pressure over the epigastrium; the stomach was only slightly enlarged. A diagnosis of old ulcer of the duodenum was made and a roentgenogram taken. It showed a niche on the internal lateral border of the bulb, confirming the diagnosis of old duodenal ulcer. It also showed all the bile ducts injected with the contrast paste, down to the finest branches of the intrahepatic ducts. The roentgenograms are reproduced. Evidently a fistula had developed into the bile tract at the site of the duodenal ulcer and had persisted for years without causing any serious clinical symptons.—*Audrey G. Morgan.*

GYNECOLOGY AND OBSTETRICS

Grunspan-de Brancas, Mathilde. La radiologie en obstétrique. (Radiology in obstetrics.) *J. de radiol. et d'électrol.*, June, 1931, *15*, 273–290.

After a brief review of the literature, the author describes the technique which is used at the Baudeloque Clinic for roentgenography in pregnancy. This is as follows: Gaiffe, Gallot and Pilon transformer, 100 ma., 120 kv., tilting table, permitting an exposure in all directions. The patient is placed in ventral decubitus (this position, contrary to what one would expect, leading to no discomfort), and the normal ray centered over the middle of the sacrolumbar articulation, the tube-film distance being 75 cm.

Roentgenography in obstetrics is of value: (1) when an assumed pregnancy cannot be diagnosed with certainty (according to the author the fetal structures are demonstrated only from the 15th to 16th week on); (2) when a pregnancy is complicated with an abdominal tumor (fibroma, ovarian cyst), or when there is a question as to the true nature of the abdominal tumor (differentiation between pregnancy and tumor); (3) when the palpation does not permit an exact diagnosis of the presentation or as to whether there is a simple or a twin pregnancy; (4) when there is a suspicion of fetal anomalies (hydrocephaly, anencephaly, etc.); (5) when the fetus is dead (the typical roentgen signs of Spalding); (6) when there is an ectopic pregnancy (in this instance an intrauterine injection of lipiodol may be of value), and (7) for the study of the position of the fetus during various phases of labor.

The roentgen examination also helps in estimating the various dimensions of the pelvis. A contracture of the pelvis may occur in the following lesions: (1) systemic bone involvement (rickets, nanism, osteomalacia); (2) claudication (unilateral, as in tuberculosis, congenital dislocation of the hip, infantile paralysis, and bilateral, as in bilateral congenital dislocation of the hip); (3) lesions of the vertebral column (true vertebral, such as humpback, scoliosis, kyphoscoliosis, and sacrovertebral, such as spondylolisthesis, spondylizema), and (4) pelvic lesions (sacroiliac, such as Naegele and Robert pelvis, and pelvic, such as exostoses, extensive callus from fractures and tumors). There are numerous procedures for pelvimetry. For the measurement of the superior strait the author recommends the method of Fabre, which is the most generally preferred. This method is described in detail. For the measurement of the inferior strait the method of Chassard and Lapiné is the most practical.—*T. Leucutia.*

GENITOURINARY SYSTEM

Hunt, Verne C. and Mayo, Charles, 2nd. Actinomycosis of the kidney. *Ann. Surg.*, Feb., 1931, *93*, 501–505.

Renal actinomycosis has been considered as primary when the disease is confined to the kidney, and secondary when other actinomycotic lesions are associated in other structures of the body. It is probable that the involvement of the kidney must be secondary to a portal of entry through mucous membrane. The extension may be direct from the gastrointestinal tract, through the diaphragm from pulmonary disease, or by metastasis through the blood stream or lymphatics.

The prognosis in general is poor. Recovery from so-called primary renal actinomycosis, when the disease is confined to one kidney, may be expected only by means of nephrectomy and the institution of therapeutic measures such as those employed for actinomycosis in other situations. A case report is included in this article.—*F. K. Alexander.*

GRAHAM, ALLEN. Pathology of renal tumors. *Radiology*, Nov., 1930, *15*, 531–541.

The paper is limited to a consideration of tumors of the kidney and perirenal region, particular attention being given to the gross pathological features which may have an important bearing upon the interpretation of roentgenograms. The more frequent types of intra- and extra-renal neoplasms and lesions simulating neoplasms are discussed briefly, and points of interest in each group are noted.

Roentgenograms of the kidney are photographic representations of the state of the organ at the time of exposure. They indicate the relative size, position, and contour of the kidney, and show relative variations in the density of the shadow of one portion of the kidney as contrasted with another, or of the kidney as contrasted with its surroundings. Additional evidence of normality or abnormality is made available by the efficient injection of opaque media, as in pyelography, which permits visualization of the calyces, pelvis, and ureter.

The cooperation that has been established between the urologist and the roentgenologist accounts in great measure for the high degree of accuracy achieved in the interpretation of variations from the roentgenogram and pyelogram of the normal kidney. The possibility of the recognition of neoplasms, extra-renal, intra-renal, or intra-pelvic, as opposed to anatomical defects, congenital malformations, and infective processes, including tuberculosis and calculus with its sequelae and complications, is very gratifying.

There are, however, certain limitations in the differentiation of the types of tumors that may be responsible for abnormal appearances in the roentgenogram or pyelogram. This is due to the fact that dissimilar types of neoplasms may present similar gross physical characteristics, and also to the fact that the same type of neoplasm may present dissimilar gross physical characteristics on different occasions and in different cases. In general, it is simpler to differentiate between a benign and a malignant tumor, which, after all, is the more important part of the problem, than it is to differentiate one type of benign neoplasm from another or one type of malignant neoplasm from another. Roentgenograms and pyelograms, alone, fall short of what is possible in the way of diagnosis when proper consideration is given to additional data such as age, clinical findings, and numerical probability.—*J. D. Camp.*

NICHOLS, B. H. Tumors of the urinary tract. *Radiology*, Nov., 1930, *15*, 547–549.

When the cystoscope cannot be introduced into the bladder, and also in those cases in which a clear field cannot be maintained in the bladder on account of persistent hemorrhage, cystography offers an easy method of determining the presence of filling defects, provided the tumor present is so large as not to be overshadowed by the remaining portion of the bladder. Tumors of the bladder are best observed by fluoroscopic cystography, as a small amount of solution in the bladder may outline the filling defect, while if the bladder is distended with fluid, the filling defect cannot be seen. Films should be made obliquely in both positions as well as anteroposteriorly.

Extensive blood clots in the bladder are sometimes mistaken for tumor filling defects. Enlargement of the prostate also produces a filling defect in the floor of the bladder. This should not be mistaken for a tumor, if it is remembered that the prostate is usually regular and smooth in outline, while tumors are irregular and asymmetrical.

Tumors of the ureter are generally of the papillomatous type and are usually transplants from a primary tumor of the kidney. They are very difficult to diagnose by the use of the ureterogram alone as stricture and other deformities produced by infection may closely simulate a tumor. A diagnosis of a primary ureteral tumor can be made only by the use of cystoscopy, close observation of the clinical symptoms, and the finding of an irregular filling defect in the ureteral lumen.

Pyelography has been found to be the best method of procedure for the diagnosis of tumors of the kidney, a method which fails only when the tumor is confined to the capsule or cortex or when there is present in the kidney pelvis a very small tumor of the papillary type, the shadow of which may be completely lost in that

of the pyelographic medium. In the latter case a pyelogram made after the injection of air will disclose a small tumor of the pelvis, but the author has hesitated to inject air into the kidney pelvis if hemorrhage has occurred, on account of the possibility of an air embolism. All other types of tumors may usually be detected by the irregularity of outline, elongation or obliteration of the calyces or pelvis. Tumors at the lower pole of the kidney may displace the ureter or obstruct it, with resultant dilatation. Benign tumors of the kidney usually show a smooth, regularly outlined deformity of one or more calyces, with displacement or compression. Such deformities may also extend to the kidney pelvis, depending upon the size and location of the growth.

Most malignant tumors of the kidney, except those of the hypernephroid type, produce an irregular filling defect indicating invasion of the kidney structure, and in any case, therefore, such findings lead to the suspicion that the tumor is malignant. It must be understood that pyelographic findings are limited to the recognition of the presence of a tumor. In only a fair percentage of cases can the pyelogram provide sufficient evidence for the differentiation between a malignant and a benign tumor. Metastases of the hypernephroid group to bones or the chest are characteristic round nodules, and will establish the type of kidney tumor if they are present.

The differential diagnosis of tumors of the kidney consists in the recognition of anomalous pelves, of a polycystic kidney, and of the presence of infection or of ureteral obstruction,with resultant hydronephrosis. Hydronephrosis in the presence of a tumor may be due either to the actual obstruction of a calyx or of the ureter by the tumor, or to a simple compression of the ureter, in which case the dilatation will be proximal to the point of obstruction. When a tumor is accompanied by hemorrhage, the presence of blood clots may produce obstruction of the ureter, with resultant hydronephrosis, which is usually accompanied by deformity of a portion of the pelvis or calyx, and may be differentiated from a general dilatation from other causes by the asymmetry of the pyelographic shadow. A hydrocalyx may be the exception, but if the entire pelvis is outlined, or if a calculus is found in a calyx, the presence of a tumor can be ruled out. Infection will seldom simulate a neoplasm. Pyelitis produces a characteristic clubbing of the calyx, and pyonephrosis produces destruction and fragmentation of the pelvis, the entire kidney usually being involved. Infection may accompany a tumor and make the diagnosis difficult. If a deformity of the pelvis is due to blood clots, this may be determined by repeated examinations, or by making a pyelogram after the pelvis has been washed out.

Congenital polycystic kidneys perhaps offer the most difficult problem in differential diagnosis, as elongation of the calyces and deformity of the kidney outline by the cystic areas may present a picture closely simulating that presented by a kidney tumor. However, in the case of a polycystic kidney a pyelogram of the opposite side will usually reveal the condition to be bilateral, while in the case of a tumor the condition is confined to only one kidney.—*J. D. Camp.*

Heckenbach, W. Roentgen findings in a case of clogged kidney. *Klin. Wchnschr.*, 1930, *9*, 1080.

A woman fifty-six years of age who had a pronounced kyphoscoliosis to the left and nephritis three years ago complained of blood in the urine for four weeks. Cystoscopy showed considerable bleeding coming from the left kidney. The roentgenogram of the kidney region demonstrated a number of typical stones in the left kidney. Pyelography showed a markedly dilated pelvis of the kidney. Nephrectomy was carried out; examination of the removed kidney revealed this to be a typical case of clogged kidney. The fine concrements were glued together by blood coagulae. Chemically they consisted chiefly of phosphoric acid and traces of oxalic acid and calcium carbonate. Two roentgenograms accompany the report.—*E. A. Pohle.*

Tourne, W., and Damm, E. On the retention of uroselectan. *Klin. Wchnschr.*, 1930, *9*, 1581; 1719.

Swick stated that five minutes following the injection of uroselectan, it could not be found in the blood. The authors contradict this statement based on blood analysis carried out in 32 cases. In their experience, the uroselectan disappears from the blood within four hours following injection provided there is normal kidney functioning. If less than half a gram was present after four hours, the kidney function

was slightly impaired; values above one-half gram speak for a higher degree of impairment. It is suggested to use the four hour value of uroselectan in the blood as a new retention test.

In the second paper, the distribution of uroselectan in the inner organs of rabbits and dogs was studied. It was present in almost all tissues. Blood, kidney, urine, liver, gall, and fur were analyzed. The kidney or liver was ligated in a number of animals. In cases of impaired kidney function, the liver took its place at least partly as excretory organ. However, the uroselectan content of the blood remained high. This indicates that the liver excretes it slower than the kidneys. In cases of impaired liver function less uroselectan is found in the kidneys; the excretion in the urine is, however, extremely high. It seems, therefore, that the kidneys can take care of the excretion by increased function. An impaired liver function is not as serious for the excretion of uroselectan as a diseased kidney. For the practice, it is well to remember not to inject uroselectan if both liver and kidneys are abnormal.—*E. A. Pohle.*

NERVOUS SYSTEM

BIANCHI, GIOVANNI. Osservazioni cliniche e radiologiche sopra due casi di "meningocele spurio traumatico" Billroth. (Clinical and roentgen study of two cases of Billroth's traumatic spurious meningocele.) *Radiol. med.*, Mar., 1931, *18*, 347–356.

Two cases of traumatic spurious meningocele are described. In both, the children suffered a trauma in infancy without any immediate disturbance of any importance. A swelling later appeared at the site of the trauma and examination showed fracture. The swelling gradually decreased in size. There was a defect in the bone of the vault of the cranium which gradually increased in size until it was much larger than would ordinarily be seen after a trauma of the same severity. The roentgen picture showed a large defect in the bone the shape of a lanceolate leaf with irregular boundaries and a tendency to linear irradiations with slight peripheral reaction. This picture suggests the condition called traumatic spurious meningocele by Billroth and traumatic cephalohydrocele by Dequervain. It is generally seen in infants after fracture of the vault of the cranium. It develops in the first few days after the injury as a subaponeurotic or subcutaneous hematoma. Normally such a hematoma is absorbed in a few days but in the cases in which traumatic spurious meningocele develops it increases in size and becomes fluctuating and pulsating. It is more or less tense, depending on the position of the patient, and increases on coughing, crying, etc. If pressure is made on it, it decreases in size and the child shows signs of cerebral compression. The swelling may reach the size of a fist and after that stops growing. In a few cases it then decreases in size and disappears; but even in the cases in which the tumor disappears the defect in the bone remains. Roentgen examination is very important in diagnosis, particularly in old cases.—*Audrey G. Morgan.*

SKELETAL SYSTEM

MCLEAN, STAFFORD. I. The roentgenographic and pathologic aspects of congenital osseous syphilis. *Am. J. Dis. Child.*, Jan., 1931, *41*, 130–152.

This is the first of a series of four papers by McLean on the skeletal lesions of congenital syphilis. He states that these lesions have been exhaustively studied by European roentgenologists and pathologists, particularly in Germany and France, but that in this country and Great Britain limited attention has been paid to the disease. His papers are based on the study of roentgenograms of the bones of 102 patients with congenital syphilis, in 24 of whom gross and microscopic examination of pathological material was made.

The histopathology of congenital syphilis is still obscured by many unsolved problems. Many debatable points exist among pathologists and roentgenologists. McLean's first paper is subdivided into the following sections: Historical data; contemporary literature; roentgenologic investigators; pathologic investigators; periostitis.

The first section, Historical Data, covers the literature of the subject from Nils Rosen's (1778) work emphasizing the value of skeletal examinations in every case of congenital syphilis to the report of von Recklinghausen (1896) on the nature of periostitic hyperostosis. He especially calls attention to the work of Parrot and Wegner, the former describing the pseudoparalysis, known by his name, and the latter, known for the first precise histopathologic description of osteochondritis which he divided into three stages. Parrot took exception to Wegner's conception of an inflammatory origin of

the syphilitic process and defined it as "dystrophy syphilitique," i.e., a nutritional disturbance of the bone tissue at the point of ossification. Parrot was the first to declare that every bone of the skeleton of infants with congenital syphilis is affected, and a localization table of lesions was made by him which has stood the test of time. Taylor (1875), the first American publication of importance, was in advance of his time in stating that because an infant was born syphilitic and in late infancy developed rickets, it was not to be deduced that syphilis was the cause of rickets. He took issue with the celebrated Parrot, who fell into the error of stating that syphilis may be considered one of the causes of rickets. McLean covers very thoroughly the controversy which raged for many years, even up to the early years of the present century, over the question as to whether syphilis was a cause of rickets.

In his section on Contemporary Literature, McLean mentions Schmidt who emphasized the epiphyseal predilection over the diaphyseal in osseous syphilis; Hochsinger who presented the first roentgen pictures of congenital osseous syphilis; Thomsen who published a complete study based on 200 cases, and numerous others.

The three outstanding roentgenologic investigators, according to McLean, are Fränkel, Alexander and Wimberger. Fränkel published his well-known monograph in 1911 which was the first systematic treatise limited to this phase of the disease. He correlated his roentgen observations with examination of pathologic material, and concluded that roentgenography is the method of choice for the investigation of congenital syphilis. In 1915, Alexander approached the subject from the same angle in a work of great detail based on a limited selection of material, largely fetal. He believed that the lesions made their appearance corresponding to the appearance of the zones of temporary ossification of endochondral origin. Asymmetries in lesions he believed were caused by asymmetric physiologic developments. He further demonstrated that periostitis in new-born infants is a persistence of fetal periostitis, which he believed did not exist without the evidence of osteochondritis. He correctly emphasized that "epiphysiolysis" or epiphyseal separation is a diaphyseal event. In 1925, Wimberger published an article which is, in McLean's opinion, the first comprehensive study of a practical nature of value alike to the roentgenologist and the clinician. He divided osseous congenital syphilis into the following types: (1) fetal syphilis, (2) nursling syphilis, (3) recidive (period of relapse) period to about the fourth year, (4) syphilis tarda, beyond the fourth year. He observed that the earliest invasion of the osseous system is at the fifth or sixth month of intrauterine life. The maximum changes in extrauterine life are manifested in the first few months, rapidly decreasing beginning with the sixth month of life. Just how late nursling syphilis occurs he believed remains to be determined. From the second and third years the lesions take on the character of acquired infection. McLean further reviews Wimberger's studies, especially with regard to the question of epiphyseal separations, the early roentgen changes at the diaphyseal ends, and the comparison of gummas of the third stage of acquired syphilis with the pathologic tissue of congenital syphilis. He also reviews the work of numerous other authors.

Of the pathologic investigators, Schmidt and Schneider stand out prominently. Schmidt as opposed to Wegner described but two forms of osteochondritis, a reactive and a non-reactive form. McLean considers Schmidt's comment on the origin of the "granulation tissue" in the severe form of osteochondritis as one of the most interesting contributions to the subject of congenital osseous syphilis. Schneider emphasized that local tissue reactions in bone lesions are actually due to the presence of the spirochete but he expressed the belief that there is no exact relation between spirochetes and tissue reaction.

The studies relating to periostitis are less convincing, McLean states, than those concerning osteochondritis, owing to the relatively smaller amount of pathologic material. Infants with the most extensive periosteal lesions as evidenced by roentgenograms are frequently in the healing stage of the disease; hence the paucity of autopsy material. In its earliest stages the lesion is of no interest to the roentgenologist, since, like the subperiosteal hemorrhage of scurvy, it gives no indication of its presence until lime deposition has begun. McLean reviews the literature very thoroughly. He warns against confusing rachitic "cloaking," periosteal reaction, with syphilitic periosteal changes. Rachitic cloaking tends to envelop both ends of the bone and the entire shaft and is uniformly distributed over all the long bones,

while syphilitic cloaking is considerably less uniformly distributed and tends to involve more heavily either the upper or the lower half of the shaft.

This paper is so voluminous that it is difficult to cover all the important contributions to the subject as reviewed by the author. It is certainly one of the most complete and authoritative reviews of the subject that has appeared in American literature for many years and is well worth serious study by every roentgenologist.—*R. S. Bromer.*

McLEAN, STAFFORD. II. The correlation of the roentgenographic and pathologic aspects of congenital osseous syphilis. *Am. J. Dis. Child.*, Feb., 1931, *41*, 363–395.

In the first of McLean's series of articles he reviewed the literature on congenital osseous syphilis. In this, the second installment, he states his chief purpose is to determine the value of the roentgenogram in the diagnosis of congenital syphilis and to correlate the roentgenologic picture with the underlying pathologic changes. His observations are based on the examination of more than 1,500 roentgen films of syphilitic infants, many of whom were studied serially. He does not assume that roentgenology will ever take the place now held by serology in the diagnosis of the disease, nor does he intend to offer the roentgenologist or the clinician a substitute for scrupulous, critical examination. He quotes Eliot, Souther and Park whose description of the phenomenon of bone growth is particularly clear. The phenomena of resorption appear to be of the first order in skeletal physiology; they dominate the pathology of bone.

The lesions situated at the junction of the shaft with the epiphyseal cartilage are usually termed osteochondritis. There has been an almost unanimous opinion among those who have written on osseous syphilis that in fetuses, as well as in infants in the first few weeks of life, a deepening in the longitudinal axis of the provisional zone of calcification in the long bones, shown on the roentgenogram as a white cap on the diaphyses and on a positive print as a dark metaphyseal band, is evidence of the syphilitic involvement of the bones. In McLean's experience the roentgenologist should be cautious about making a diagnosis of syphilis on this evidence alone, and the pathologist might be equally confused unless he was able to demonstrate spirochetes in the lesions, a difficult matter in infants who have lived for some weeks, but less difficult in fetuses. The roentgenologist who makes such a diagnosis may be right, but he must bear in mind that other conditions may cause such an appearance of the diaphyseal end and he cannot make an unequivocal diagnosis of syphilis on this roentgen evidence alone. McLean has noted these changes in four instances in non-syphilitic infants and he feels that one cannot state that the actual lesion is a local specific one due to the presence of the spirochete even in a syphilitic infant, since the widening of the provisional zone of calcification may be due to the growth-retarding effect of the syphilitic virus on the organism, even as starvation unfavorably affects the impulse to growth.

The pathological changes that are responsible for the above roentgen appearance are a widened and broader zone of provisional calcification which is whitish yellow in color instead of pink, and which feels gritty to the probe. McLean describes the microscopical appearance in detail, adding that the diaphyseal machinery for the production of bone has had the normal quantity of raw material available, in the form of calcified intercellular ground substance, for the manufacture of bone, but some inhibitory influence has disturbed the automatic levers (the blood vessels of the shaft) which bud out from the shaft to the proliferating cartilage and encase the calcified ground substance with osteoblasts and convert it into bone. The substance that has disturbed this delicate mechanism may be the syphilitic virus. In consequence, the unused raw material (the calcified intercellular ground substance) piles up at the metaphysis and explains the dense white shadow shown by the roentgen rays at the end of the bone.

In the early stage of osteochondritis there is not infrequently an associated widening (in its longitudinal axis) of the cartilage proliferation zone. Less frequently there is a reduction of the proliferations of cartilage which seems to lead to widening of the horizontal septums of the cartilage ground substance.

The next stage in order of severity of the lesions at the epiphyses shows on the roentgenogram a very slight or very marked degree of submetaphyseal rarefaction, either with or without the deepened provisional zone of calcification. From the observations of previous

authors and his own experience, McLean feels that widening of the zone of provisional calcification and even submetaphyseal rarefaction may not be due to local action by the spirochetes but to the systemic effect of the disease on the blood. It is well known that infants with congenital syphilis frequently have secondary anemia. It is not impossible that severe anemia in certain cases might be a contributory factor in the production of such changes.

The submetaphyseal rarefaction is visible on the roentgenogram because of the deficient subchondral formation of spongiosa due either to a diminution in the number of new trabeculae or to their immature development. The lessened number of trabeculae is probably due to the fact that osteoblastic activity has not ceased with sufficient abruptness entirely to prevent vascular loops from the shaft from converting calcified ground substance into bone. The trabeculae thus formed are relatively few as compared with normal bone and are thin because the defective osteoblasts have not been able to entirely complete their task.

There is a more advanced stage of osteochondritis in which the roentgenologist can usually make an unequivocal diagnosis of osseous syphilis in the presence of a negative serology and the history of a negative physical examination. The sign of this stage is the so-called zig-zag or saw-tooth metaphysis type of lesion which is not uncommon, especially if the roentgenologist examines the film with a reading glass. As opposed to the lesions previously described, these might be called, McLean states, active or specific lesions, since they are seen only when connective tissue is present and active resorption comes into play. However he warns against accepting the presence of one or possibly two minute spurs or buds shown on the metaphysis in the roentgenogram as evidence of syphilis, since they also occur in rickets. Even in true syphilitic types cupping similar to that seen in rickets may be present. This saw-tooth edge is visible only on its epiphyseal side, the side toward the joint, because of its transparent background. There are also tongue-like protrusions toward the diaphyses, away from the joint which are usually made up of groups of columnar cartilage cells which either because of excessive growth or because of diminished osteoclastic and osteoblastic activity have piled up at the epiphyseal-diaphyseal junction and have invaded the diaphysis at its weakest points. Since they seldom contain lime salts these columns of cartilage cells are not often demonstrable by the roentgen rays.

McLean is of the opinion that the so-called granulation tissue is probably not of a specific character and he rather doubts that it is a specific inflammatory tissue. When the roentgenogram shows rarefaction, connective tissue is present, and the roentgenograms of more advanced stages of osteochondritis are fairly representative in the order of severity of the amount of connective tissue present. Roentgenograms may show only foci of rarefaction at one or both angles of the epiphyseal-diaphyseal junction, a deep area of rarefaction between the shaft and epiphyseal cartilage with only thin strands of cortex or trabecular structure uniting the proximal and distal fragments of the shaft, or a wide rarefied zone between the shaft and epiphyseal end with displacement or impaction with or without angulation of the latter. Not infrequently the roentgenogram shows that as much as one-fifth of the end of the shaft, usually the distal end, has apparently melted away.

"Epiphysial separations" as demonstrated by the roentgen rays are in reality usually breaks in the ends of the shafts. Only rarely does the roentgenogram demonstrate a true epiphyseal separation. These breaks are due to weakness of structure and take place in the stratum of intercellular ground substance, a stratum of weak, brittle and immature bone. With the intercellular ground substance are found groups of columnar cartilage cells, connective tissue and trabecular structure with diminished or entirely absent osteoblasts. If separation does not occur in this brittle stage, it may occur through the zone of connective tissue. It is not really the presence of connective tissue that invites separation but the disorder which precedes its growth.

Periostitis as a sole lesion is seldom found, consequently it is of less diagnostic importance than osteochondritis. McLean describes three types of periostitis:

1. Periosteal thickening which occurs in an intact shaft independently of the lesions at the metaphysis, generally thickest in the middle of the shaft.

2. A supportive or healing type which is found over any break in the cortex of the shaft.

3. Ossifying periostitis or the hypertrophic osteoporosis of Pehu, which is the least common of all the types and is characterized by a

tremendous thickening of the entire shaft of the bone, due to a series of enveloping coatlike layers of newly formed bone which are separated from the shaft and from each other by a thin layer of spongy substance.—*R. S. Bromer.*

McLEAN, STAFFORD. III. Correlation of the roentgenologic picture with the gross and the microscopic examination of pathologic material in congenital osseous syphilis. *Am. J. Dis. Child.*, Mar., 1931, *41*, 607–675.

In the third section of McLean's study of congenital osseous syphilis he presents an abstract of the charts of 16 syphilitic infants who came to autopsy. The youngest was one month and the oldest thirteen months of age. Thirteen were not over three months.

In each of the 16 cases, evidence of pathologic changes in the bones was noted in the roentgenogram. In all but 2 instances the bone removed at autopsy for microscopic examination was selected because it presented the most marked evidence of the disease in the roentgenogram. The specimens offered for study ranged from the cases showing the earliest changes in the bone at the epiphyseal-diaphyseal junction to the most advanced type of osteochondritis showing extreme lawlessness of growth. The diaphyseal lesions ranged from slight changes in the cortices to well-marked, symmetrical osteomyelitic lesions involving a large area of the shaft. A number of the cases showed periosteal changes. The specimens consisted of nearly every variety of pathologic change of the bone in congenital syphilis of the first few months of life. The paper is profusely illustrated with roentgenograms illustrating all varieties of lesions.

McLean states that after scrutinizing a roentgenogram of a syphilitic infant with the naked eye and the reading glass, the careful study of the material presented should enable one to have a fairly complete picture of the underlying pathologic changes.

The case histories are given with such detail both in regard to roentgenologic and pathologic findings, that they offer to roentgenologists a comprehensive and thorough review of the subject.—*R. S. Bromer.*

McLEAN, STAFFORD. IV. The correlation of the clinical picture with the osseous lesions of congenital syphilis as shown by the x-rays. *Am. J. Dis. Child.*, May, 1931, *41*, 1128–1171.

This is the concluding paper of McLean's series on the clinical, roentgenological and pathological study of congenital syphilis. In them he has correlated the various findings by the different methods of investigation, pathological, clinical and roentgenological. This installment consists of case reports which are voluminously illustrated with clinical photographs and roentgenograms.

This series is of extreme importance to roentgenologists, inasmuch as nowhere can they find such material presented in a logical and correlated fashion, as McLean has done. In addition, the first paper contained an historical account of previous investigations of congenital syphilis with an extensive bibliography. The series of papers should be included in the reference library of all roentgenologists.—*R. S. Bromer.*

PARK, EDWARDS A., JACKSON, DEBORAH, and KAJDI, LASLO. Shadows produced by lead in the x-ray picture of the growing skeleton. *Am. J. Dis. Child.*, March, 1931, *41*, 485–499.

The authors observed in the course of study of roentgenograms of many bones of children, removed after death, that the ingestion of lead may cause shadows to appear at the growing ends of the long bones similar to those seen after continued administration of phosphorus as had been previously reported by Wegner and Phemister. Like elementary phosphorus, arsenic and perhaps some other heavy metals, lead can cloud bones in the roentgenograms, the clouding being most conspicuous where growth is occurring most rapidly, namely, at the anterior ends of the middle six ribs, the lower ends of the radius and ulna, at both ends of the tibia and fibula, and the lower ends of the femora. That only those parts of the skeleton in process of growth at the time of ingestion of lead are affected is proved by the entirely normal structure of the old bone proximal to the lesions, the sharp limitation of the lesions to the growing parts and a degree of involvement at any point exactly proportional to the rate of growth at that point. Obviously growth in any bone takes place in many places, but only where growth occurs rapidly do the changes readily reach such magnitude as to show in roentgenograms.

The fact that only the bone in process of growth is affected must mean that the lead either enters into chemical composition of the bone or influences cellular activity in such a

way that the character of the bone becomes altered. So far as Park and his coworkers could determine from two of the cases studied by them, the lead modified endochondral ossification in such a way that the trabeculae formed under the cartilage a much more dense thicket than normally, and these formations of densely packed trabeculae were the cause of the band-like shadows. On the other hand, they admit the probability that lead itself was in the trabeculae and that it may have been partly responsible for the shadows.

In the first two cases reported by them, the shadows were narrow and intense, the children were young, and death occurred. From the fact that death took place and that the shadow in the bone was intense, one might think that the amount of lead eaten was large, and from the fact that the band was narrow one might infer that the period of poisoning was of short duration. In their third case no history of lead poisoning could be obtained, although the evidence of the condition in the child was entirely satisfactory. In the fourth case the history indicated that the eating of lead had been marked for one year. The shadows in the bones of this child were not as heavy as the history might suggest, but their breadth (from 1 to 1.5 cm.) was in keeping with the long duration of the poisoning, and their position just under the cartilage corroborated the statement that the habit of eating lead continued up to the time when the roentgenograms were taken.

The authors state that there are pertinent questions they cannot answer. Since the phenomenon seems to be dependent on growth, one would expect it to occur less and less frequently with increase in age, and never to occur in the fully grown person. They feel certain from theoretical considerations that lead can affect the skeleton in the way described only in the case of children, and they believe that the phenomenon will be the more strikingly developed the younger the subject. Another question is the constancy of the phenomenon in cases of lead poisoning in children. They do not believe that the shadows will be found in all cases, though they guess that they will be found in most cases of severe poisoning in young children. At any rate they conclude that the clouding of the rapidly growing ends of the long bones as seen in roentgenograms ought to be a useful, corroborating, or perhaps suggestive, sign of lead poisoning in children.—*R. S. Bromer.*

Ledoux, E., and Cottet, P. Enchondromes multiple associés à des exostoses ostéogéniques chez un enfant ayant présenté une hypertrophie du thymus. (Multiple enchondromata associated with exostoses in an infant who had previous hypertrophy of the thymus.) *Bull. et mém. Soc. méd. de hôp. de Par.*, Feb. 23, 1931, *55*, 261–264.

The authors present a case of multiple enchondromata associated with previous thymic enlargement. Their patient was eight years of age, presenting typical enchondromata, who from birth up to the age of eight months, had shown symptoms of thymic enlargement. They state that naturally the question arises whether the thymic enlargement was a causative factor in the development of the enchondromata. They quote Ugo Soli who claims that thymectomy in animals causes alterations in the growth of the epiphyses. Lucien and Parisot, on the contrary, found this in only one of many animals in which the thymus had been removed. Rachitic deformities have been associated with thymic hypertrophy. Huber has lately suggested an endocrine disturbance as a cause of multiple enchondromata. The authors attempt no answer to the question of the part that thymic hypertrophy may play in the causation of multiple enchondromata.—*R. S. Bromer.*

Faulkner, D. M. Tuberculosis and Köhler's disease. *J. Bone & Joint Surg.*, April, 1931, *13*, 369–372.

In 1923 Greenwood reported a case of Köhler's disease of the scaphoid in which the roentgenogram showed the usual typical picture of the condition, but in addition a tiny sequestrum could be seen lying near a corresponding hollow in the scaphoid. Recovery ensued under conservative treatment, but as the patient's parents had pulmonary tuberculosis and the patient later developed it, Greenwood believed that *Bacillus tuberculosis* was the causative agent. In a later communication he reports a second case which when first seen was typical of Köhler's disease, but which progressed to a terminal condition of tuberculosis of the tarsus. He concludes that Köhler's disease is due to a blood-borne infection of low pathogenicity, that this name has been applied to an early and abortive infection of the tarsal scaphoid by the *Bacillus tuberculosis*, and that the term "tarsal scaphoiditis" is in accordance with the known pathology of the disease.

Faulkner reports a case in which Köhler's disease was present. Following an acute upper respiratory infection, osteitis of the tarsal scaphoid was found, which at operation later was proved to be due to *Bacillus tuberculosis*. Whether this helps to confirm Greenwood's contention that *Bacillus tuberculosis* is the cause of Köhler's disease or whether this case was merely tuberculosis occurring in a congenitally anomalous tarsal scaphoid, cannot be decided without further experience. Faulkner's case report is well illustrated with roentgenograms.—*R. S. Bromer.*

LAPIDUS, PAUL W. Fracture of metatarsal bones simulating thrombo-angiitis obliterans. *J. Bone & Joint Surg.*, April, 1931, *13*, 366–369.

Lapidus reports a case of fracture of the second, third, and fourth metatarsal bones with hemorrhage between the fragments at first, and callus formation later on, causing compression of the second and third metatarsae dorsales and plantares. The third toe suffered more than the others from lack of blood supply because all four of its arteries were located between the fractured metatarsal bones. Thus local impairment of circulation had to be dealt with, together with all its consequences, pain, gangrene, etc. This condition resembled so closely the one observed in thrombo-angiitis obliterans that this diagnosis seemed to be justifiable on the first examination. However the absence of intermittent claudication with pain in the calves after a short walk, usually observed in cases of thrombo-angiitis obliterans, and the presence of good pulsation in both dorsalis pedis arteries made this diagnosis questionable.—*R. S. Bromer.*

MILLER, OSCAR LEE. Plastic bone repair after therapeutic irradiation. *J. Bone & Joint Surg.*, April, 1931, *13*, 329–333.

Miller reports a case showing impairment of bone growth after therapeutic irradiation and experience with its surgical management. Apparently opportunity to do plastic surgery after such therapy has been somewhat limited. This may suggest that not a lot of irradiation has been prescribed in the young, or if prescribed, the lesion under treatment proved fatal or was entirely healed. Certainly, not a great deal of a practical nature has been reported on the behavior of bone tissue where plastic surgery has been required to repair defect in a sharply radiated zone.

The original lesion in Miller's case was a bone cyst in the tibia and the patient sustained a fracture at the site of the lesion. If the lesion was malignant it was entirely cured, evidently, by radium treatment. There resulted, however, an irradiation osteitis, secondary infection in the tibia and non-union. At no time after the patient was admitted to the author's clinic did the involved tissues have the appearance of an osteomyelitis of the usual type. Drainage, when present, appeared to be coming from a source of tissue death, rather than from active infection. The roentgen appearance of the irradiated tibia ends suggested poor viability. Following the first operation the bone ends, though not uniting, appeared more viable. The technique carried out in the first bone-graft operation should have been successful in the average case of non-union of the tibia.

The success of the second operation was due either to the fact that a certain necessary length of time had elapsed since irradiation and the bone had recovered viability, or the changed surgical approach which was used, found the tissues more receptive. In the later approach the tissues had not been disturbed by former surgery and were on the opposite side of the bone from the applied radium. Miller concludes that it is certainly safe to assume that early after irradiation is not the ideal time to undertake plastic bone surgery.—*R. S. Bromer.*

FREUND, ERNST. Zur Frage der Femurkopfverunstaltung nach unblutig eingerenkten angeborenen Hüftgelenksluxationen. (On the question of deformity of the femoral head following closed reduction of congenital dislocation of the hip joint.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1931, *43*, 131–168.

About 1000 cases of congenital dislocation of the hip joint have been observed during the past five years at the Rizzoli Orthopedic Institute of Bologna under the directorship of Professor Putti. Of these, 20 were roentgenologically examined at repeated intervals for the study of late deformities of the femoral head, 13 being described in detail in the present article and illustrated with 56 figures.

It was found that most of the late deformities of the femoral head were the result of a process occurring within the joint following reduction. This could be traced back to two different conditions, the one being osteochondritic and the other arthritic in nature. The two conditions

have nothing in common as regards the course of the disease but they may occur simultaneously as coordinated sequelae of the dislocation of the hip. In both instances the presence of a constitutional factor must be assumed. In the osteochondritic form the slight trauma following reduction leads, most probably through compression of the epiphyseal nucleus, to an aseptic necrosis of the epiphyseal spongiosa with consecutive regeneration, such as described by the author in osteochondritis of Perthes' disease. In the arthritic form the fixation of the epiphyseal head in the acetabular cavity is the provoking cause. Whereas the osteochondritic form always leaves the articular cartilage intact, in the arthritic form there is an involvement of the cartilaginous surface from the earliest stages this extending later, with increased mechanical function of the joint, to the subchondral spongiosa, occasionally leading to entire disappearance of the epiphysis of the femoral head.

The roentgenologic differentiation of the two forms encounters as a rule no difficulties. From the clinical standpoint a surprisingly slight symptomatology as compared with the marked changes found in the roentgenograms is characteristic. It is recommended that in all instances roentgenograms be taken six months after the completion of the treatment to note if there is any further progression in the deformities of the hip joint. Should this be the case further immobilization is indicated.

Aside from the above osteochondritic and arthritic changes the author noticed on the roentgenograms taken following the completion of the immobilization, two parallel calcification bands appearing in the juxta epiphyseal portion of the femoral neck. The distance between the two bands was nearly always identical with the distance between the proximal calcification band and the epiphyseal line. From this the author concluded that the two bands were the result of the normal enchondral ossification during the period of immobilization, the distance between the two bands corresponding to the three months of the first phase of immobilization in the first Lorenz's position and the distance between the proximal calcification band and the epiphyseal line corresponding to the three months of the second phase of the immobilization in the second Lorenz's position.—*T. Leucutia.*

Piergrossi, Aldo. Su di un caso di osteosi eburneizzante monomelica (Meloreostosi). (On a case of eburnizing monomelic ostosis (melorheostosis).) *Arch. di radiol.*, Jan.–Feb., 1931, *7*, 20–50.

The author describes in detail and illustrates with several roentgenograms a case of melorheostosis of the right lower limb which occurred in a man thirty-six years of age. The chief characteristics were a hyperostosis, "flowing" at the external or internal aspect of the bones of the entire right limb, from the iliac fossa to the terminal phalanges of the last three toes; monomelic involvement; elongated appearance of the osteosclerosis in the diaphysis, and a rounded appearance in the epiphysis and short bones; interspersed areas of rarefaction and heterotopic ossification. It is probable that the disease had two successive phases; in the first, the osteosclerosis with practically no change in the contour of the bones, and in the second the periostosis with marked deformity of the contour of the bones predominating. In discussing the various theories of etiology, the author stresses that of Putti which attributes the changes to disturbances of the sympathetic.—*T. Leucutia.*

D'Amato, Giuseppe. Su alcune particolari formazioni che si riscontrano nella spongiosa metafisaria delle ossa lunghe. (Some structures found in the spongiosa of the metaphyses of the long bones.) *Radiol. med.*, Mar., 1931, *18*, 315–325.

The author describes some calcareous deposits and islands of bone condensation which he found in studying the spongy substance of the long bones, chiefly in the metaphyses; in other places he found cystic foci with a peripheral border of sclerosis. These lesions were found in healthy parts of the long bones in subjects who had tuberculosis of other parts of the skeleton or of other organs; the tuberculosis was not causing any subjective or objective symptoms. The author thinks that the first class of changes were residues of foci of embolic or traumatic necrosis and that the latter were residues of old tuberculous foci, the development of which had been arrested by prompt and energetic local defense.—*Audrey G. Morgan.*

Blaine, Edward S. Spondylitis traumatica tarda (Kummell's disease). *Radiology*, Nov., 1930, *15*, 551–561.

The principal feature in the discovery of a case of spondylitis traumatica tarda is the finding roentgenologically of a more or less collapsed vertebral body, often without kyphos or knuckle; it may be incident to an examination for non-traumatic lesions. There is often no recollection of a severe back injury, but in other cases there is a history of such an event several months to several years previously, often not of enough severity to have put the patient to bed or call for more than casual medical attention. Such injuries consist of a more or less severe squeezing force to the upper and lower parts of the patient's body in hyperflexion. The bone collapse was not present immediately after the injury, as shown on roentgen examination at the time, or, in the absence of such roentgen examination, as based on the absence of clinical evidence of a fractured vertebra. The particular cause of the changes which characterize this lesion appears to be a trauma to the trophic supply of an individual vertebra by which this vitally necessary mechanism is prevented from functioning, thereby disturbing the normal process in maintaining the integrity of an individual bone. This, then, is followed by the absorption of devitalized bone cells in greater or lesser amount, in accordance with the amount of trophic injury incurred. Lacking the repair process, an absorption of the devitalized bone takes place, the volume of the bone decreases, and the result is a lessening in the size (volume) of the body of the involved vertebra. This is seen on the roentgen film as shadows that represent a "settling" process, demonstrated by the decrease in height.

The roentgen shadow outline of the involved vertebral body has changed from that of a fairly regular parallelogram to that of a truncated cone, which is graphically shown on the lateral roentgen projection in such cases. Incidentally, it is to be remarked that this lesion is seldom recognized on the anteroposterior roentgen projections, even on technically perfect films, but after finding the lesion on the lateral projection it will be recognized and supported by shadows on the anteroposterior views, particularly on stereoscopic visualization.

The principal lesion to be differentiated from Kümmell's disease is spondylitis tuberculosa. In this condition there is suppuration, necrosis, and much more absorption of bone tissue than is usual in Kümmell's disease, the gibbus is invariably much more pronounced, and the condition is vastly more painful. In fact, many cases of Kümmell's disease do not develop a knuckle, the loss being more even throughout the bone, which results in a more even settling. Spondylosa rhizomelica, post-typhoid spine, malignancy of the spine, syphilis of the spinal bones and osteomalacia must also be differentiated.

Ten case reports are presented.—*J. D. Camp.*

TALIA, FERDINANDO. Emisacralizzazione dolorosa d'una sesta vertebra lombare. (Painful hemisacralization of the sixth lumbar vertebra.) *Arch. di radiol.*, Jan–Feb., 1931, *7*, 56–61.

An interesting anomaly of the lumbar spine, consisting in the presence of a sixth lumbar vertebra with hemisacralization on the right side, is briefly described. The patient suffered considerable pain which was of a sciatic character. It is probable that this pain was the result of the partial sacralization.—*T. Leucutia.*

CODMAN, ERNEST A., and AKERSON, IRVING B. The pathology associated with rupture of the supraspinatus tendon. *Ann. Surg.*, Jan., 1931, *93*, 348–359.

The authors believe that rupture of the supraspinatus tendon is the most common of prolonged shoulder disability in industry and one which is most always overlooked. With this condition, the patient gives a history of considerable trauma; he can raise his arm only with great effort, if at all; there is lack of normal scapulo-humeral rhythm; there is a tender point corresponding to the insertion of the supraspinatus where a slight sulcus and a slight eminence can be felt; there is a painful jag and characteristic crepitus as this tender point disappears beneath the acromion as the arm is elevated. There is no roentgenologic method of diagnosing this lesion.

The incidence of rupture in the authors' series is given as 39 per cent with four hypotheses to explain the lesions found: (1) They may be the result of trauma (i.e., rupture of tendon fibers, followed by imperfect repair); (2) the defects left as a result of so-called "calcified deposits"; (3) the result of necrosis of the tendon or other diffuse pathologic process, or of the same phenomena which are known as arthritis in other joints, and (4) the direct result of attrition.

In favor of the traumatic origin is the clinical symptom-complex, microscopic sections indicating loss of continuity of the fibers and the preponderance of the right over the left. Against a traumatic origin is in the tissue removed from tendons of aged people in this region and from cases operated upon, whether traumatic or not, which show a necrosis the result of retrograde changes; 14 per cent of bilateral cases found at autopsy speak against traumatism and favor slow necrotic destruction. The authors do not subscribe to the theory of attrition and are inclined to think that changes in the integrity of the tendon due to age, constitutional conditions, or over-use are primary as a rule, but that trauma produces the actual rupture in most cases.—*F. K. Alexander.*

Coley, William B. Multiple myeloma. *Ann. Surg.*, Jan., 1931, *93*, 77–89.

The author prepared this paper primarily to stress the treatment aspect of multiple myeloma, as the fatal outcome of the disease has been so universally accepted that the question of treatment is scarcely referred to in the very considerable literature on the subject.

Multiple myeloma is, in most cases, highly sensitive to both the toxins of erysipelas and *Bacillus prodigiosus* and to radiation. Furthermore, the inhibitory action of these two agents is not only sufficient to cause great amelioration of the symptoms, in most cases, but the disappearance of the tumors, in a few cases with apparently a lasting cure.

The clinical appearances of multiple myeloma are rather definite and enable one to make a diagnosis in the majority of cases. The characteristics are as follows: (1) Tumor—originating in the cancellous portion or in the marrow of the bone. (2) Site—areas of predilection are the usual, the spine, rib, humerus, femur, knee and pelvis are affected most often in the early stages of the disease. (3) Multiple foci, which may have existed from the very beginning. (4) Pathological fracture due to the bone-destroying characteristics of the tumor. (5) Paraplegia in case the spine is involved. (6) Bence-Jones bodies. (7) Nephritis. (8) Anemia.

The roentgen appearance is that of multiple "punched-out" areas of bone destruction. If the disease starts in one of the long bones, first as a solitary lesion, a plasma cell myeloma, the roentgenogram may closely resemble that of an endothelial myeloma.

The etiology is as yet unknown.

The differential diagnosis is primarily from endothelial myeloma. In both conditions the disease, if not multiple when first seen, soon shows multiple lesions. In both, the trouble starts in the marrow of the bone and destroys adjacent bone. In multiple myeloma this destruction is less widespread and causes an early pathological fracture. Endothelial myeloma is a disease usually found in young adults, while multiple myeloma occurs more commonly after forty. Giant cell tumor and metastatic carcinoma at times resemble multiple myeloma.

The author reports several cases of multiple myeloma which had been treated by radiation and toxins showing that the disease may be held in check by a combination of these therapeutic methods, and maintains that no case should be given up as hopeless without a prolonged thorough trial of both toxins and radiations.—*F. K. Alexander.*

Knoll, W., and Matthies, Th. Darstellung von Gelenken mittels Jodipinfüllungen. (Visualization of joints by means of iodipin filling.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1931, *43*, 85–91.

The authors injected the articular cavities of the ankle, knee and elbow joints in a number of cadavers with iodipin and found that the process can be used to advantage for the demonstration of the anatomic relation of the bones to the joint capsule. With improvement of technique, the method might be applied also in the living.—*T. Leucutia.*

Copeland, Murray M. Bone metastases. *Radiology*, Feb., 1931, *16*, 198–210.

Three hundred and thirty-four cases of malignant metastasis in bone were studied by the author. Of these, 100 cases were consequent to cancer of the breast. The bones most frequently involved in order of incidence were the spine, pelvis, femur, skull, ribs and humerus; metastasis in the forearm and leg was infrequent. The lesions were most often multiple, and were single in only one-fourth of the cases. Metastasis occurred in 22 cases of hypernephroma; bones affected, in order of frequency, were the humerus, spine, femur, pelvis, ribs, bones of the feet, skull, sternum. Cancer

of the prostate produced metastasis in 134 cases and most frequently involved the pelvis and vertebrae, rarely the femurs, lower end of the tibia, and the skull. Malignant disease of the testicle was the primary source in 2 cases, of the bladder in one, of the ovary in 2 and of the thyroid in 6. Seven patients with cancer of the stomach had metastasis to the bones, the order being ribs, pelvis and femur, vertebrae, sternum, skull and scapula. Metastasis to bone was found in 4 cases of cancer of the lung; a wide variety of bones were involved, including the lumbar spine, pelvis, ribs and skull.—*J. D. Camp.*

GENERAL

AUBERTIN, CHARLES. Poussées leucocytaires chez un radiologiste. (Recurrent leucocytosis in the blood of a radiologist.) *Bull. et mém. Soc. méd. de hôp. de Par.*, March 2, 1931, *55*, 307–310.

Aubertin states that the relative frequency of leucemia in radiologists in his experience (5 radiologists and only one other physician), seems to be more than mere coincidence. The importance of determining whether radiologists were more prone to leucemia than other physicians, led him to study carefully the blood of a roentgen technician who had been exposed to a considerable amount of roentgen irradiation, small repeated doses. Previously he had never observed any leucocytosis in persons exposed to roentgen rays which could not be explained by an acute infection. On the contrary, the usual change in such persons is a leucopenia with a tendency to a low polymorphonuclear count. Aubertin's case reacted with a decided increase in leucocytes (36,800) but with no leucemic changes. This diminished slowly during a period of ten months following cessation of roentgen exposure, to about 10,000. At the time of the high leucocyte count a few myelocytes and nucleated red blood corpuscles were present. More than a year later, the patient having had no further roentgen exposure, a count of 28,000 was obtained. After a four months' interval this second leucocytosis again disappeared.

Aubertin does not consider that this phenomenon is to be interpreted as a pre-leucemic stage, but he thinks it should be regarded as an effect of chronic, repeated small doses of roentgen radiation. He has also observed this same effect in animals irradiated with small repeated doses.—*R. S. Bromer.*

KIRKLIN, B. R., and MORTON, S. A. Roentgenologic changes in sarcoid and related lesions. *Radiology*, March, 1931, *16*, 328–333.

Boeck's sarcoid, which is characterized by the formation of nodules in the cutaneous and subcutaneous tissues, sometimes associated with fibrocystic changes in the bones or a fibrous infiltration in the lungs, is generally regarded as a form of infection with the bacillus of tuberculosis, although other hypotheses as to its origin have been advanced. The authors have reviewed the roentgenologic observations in 6 cases, of which 2 had demonstrable changes in the bones, 2 in the lungs, and 2 in both the bones and the lungs. In the lungs the typical abnormality is a bilateral, fairly dense, diffuse, linear infiltration of the midportion or bases, superimposed on which are discrete opaque areas, ranging in size from miliary nodules to nodules 1 cm. in diameter. The apexes are not affected and there are no signs of pleurisy or fluid. Of the bones the phalanges of the hand or foot are most often attacked. The disease of the bone seems to be first evident as a thickening of the trabeculae in the end of the phalanx. Punched-out areas appear and later there is a peculiar combination of destruction and repair. The whole phalanx may be affected. If the process is arrested and healing occurs the bone may return almost to normal, but usually considerable mutilation results.—*J. D. Camp.*

WARTHIN, ALDRED S. The genetic neoplastic relationships of Hodgkin's disease, aleukaemic and leukaemic lymphoblastoma and mycosis fungoides. *Ann. Surg.*, Jan., 1931, *93*, 153–161.

The author believes that Hodgkin's disease is a neoplasm and related genetically to the lymphoblastomas, of which both the aleucemic and leucemic forms have identical pathology; and that mycosis fungoides is likewise a neoplasm belonging to the same generic group. The essential differences between these different clinical forms consist in different degrees of differentiation or entdifferentiation, and the organ or tissue primarily involved. Transition forms exist between all these groups, and one form may be transformed into another.

The clinical picture of the disease as a whole is presented, with statements to the effect of the unknown etiological factors.

The characteristic and easily recognizable

histological picture presents a localized or focal proliferation of the reticulum with the presence of atypical lymphocytes, lymphoblasts, plasma cells, mononuclear and polynuclear eosinophils and the multinucleated "Hodgkin's" or "Dorothy Reed" giant cells, which resemble those of the bone marrow. These and the eosinophil cells constitute the chief diagnostic factors microscopically; and the diagnosis of typical Hodgkin's rests upon their presence and is never made in their absence.

As the disease becomes chronic the structure of the node is wholly lost, and its appearance becomes that of a multicentric nodular mass. In the more actively growing cellular forms, degeneration and necrosis occur frequently; often these degenerative processes are so marked that a great reduction in their size, even to that of the normal node, may result.

As atypical Hodgkin's are those cases in which the atypical myeloid cells, "Dorothy Reed" cells and eosinophil cells are either few in number or are absent. The focal or nodular replacement of the lymph nodes by fibrous connective tissue or atypical lymphoid tissue, with all of the clinical picture of Hodgkin's, constitutes the basis for the diagnosis of Hodgkin's and clinical observation confirms this in the majority of cases. For the greater part, this group represents transition forms to the reticulocytosarcomatous type of lesion.

By sarcomatous Hodgkin's is meant very actively growing, diffusely cellular rather than nodular lesions with few or no eosinphils or "Dorothy Reed" cells, and a great tendency to infiltrate and metastasize, particularly in the kidneys and the lungs. The sarcomatous degeneration of a Hodgkin's may proceed in one of two directions, either leading to a lymphosarcoma or to a large-celled form with abundant reticulum and numerous giant cells, which has been named a reticulcytoma or reticulo-endothelioblastoma. The former rises through the overproduction of maternal lymphoblasts, the resulting growths being typical lymphoblastomas, either small celled or large celled. Usually the resulting lymphoblastoma is aleucemic but the gradual developing blood picture of a leucemia of the lymphatic type is not uncommon. In the reticuloendothelial blastoma type, the lymphoid cells become reduced in number, the eosinphils disappear and the majority of cells come to be large polymorphic cells with an abundant cytoplasm, and possessing many large hyperchromatic nuclei. This form shows a greater degree of malignancy than either the type of Hodgkin's or the lymphoblastoma. It is especially likely to develop metastases in the kidney, and the spleen is involved earlier than in the other two forms.

Mycosis fungoides in a great majority of cases is a small-celled lymphoblastoma involving the primitive lymph nodes of the papillary layer of the dermis but ultimately coalescing to form the fungoid tumors of the skin, becoming generalized at last in all of the lymphoid tissues of the body. It may become leucemic, or may be associated with a leucemia from the beginning (leucemia cutis). Aside from the skin nodes which may precede or follow that of the regional lymph nodes, the pathologic picture is that of a generalized lymphoblastoma.

There is but one method of treatment which will delay but will not halt the inevitable malignant progress of these growths, and that is the judicious and systematic employment of roentgen irradiation.—*F. K. Alexander.*

ROENTGEN AND RADIUM THERAPY

Kaplan, Ira I. The emergency value of roentgen therapy in pediatrics. *Arch. Pediat.*, May, 1931, *48*, 330–334.

By many persons, in both the profession and among the laity, the emergency use of the roentgen rays is considered to be their employment for the examination of fractures of the bones. The use of the roentgen rays for therapeutic purposes has always been regarded as a slow, tedious, long-drawn out means of handling diseases mostly of a malignant nature. Kaplan however does not agree with such views. He points out the use of the roentgen ray in the treatment of the enlarged or persistent thymus. He also used the roentgen rays in the emergency treatment of a case of lymphosarcoma of the chest which may have originated in the thymus gland. His patient showed marked improvement within twenty-four hours after one treatment. Comparison of roentgenograms made after the treatment showed almost complete recession of the mediastinal growth. In cases of sarcoma of the kidney and pelvis in children roentgen therapy by shrinking the tumor mass relieves the usual pressure symptoms and makes the patient more comfortable as in the case of the lymphosarcoma just quoted. If the

treatment is begun early enough in the course of the disease, prolongation of life with comfort is quite possible. In the case of a bone condition, whether the lesion be benign or malignant, roentgen therapy may relieve the pain. For tuberculous adenitis the roentgen rays offer a very excellent method of reducing the swellings of the gland without surgical interference. In young girls they are useful in the treatment of toxic goiter and in young children where the enlarged leucemic adenopathy by its pressure on vital organs tends to bring on a hasty death, the therapeutic use of roentgen rays over the swollen lymphatic areas and the spleen gives remarkably quick relief. It is also useful in Hodgkin's disease for the immediate relief of urgent symptoms.—*R. S. Bromer.*

REGAUD, CL. Quelques particularités de la vie des tissus cancéreux mises en évidence par la radiothérapie. (Some peculiarities of the life of cancerous tissues as evidenced by radiotherapy.) *Arch. Inst. du Radium de l'Univ. de Paris*, *2*, 371–383.

The growth of cancerous tissue in a typical epidermoid epithelioma occurs between the zone of multiplication (the peripheric mother cells) and the zone of desquamation (the central squamae which represent terminations of the sterile cellular lines). In other types of cancer, the mother cells and the cells of the sterile lateral lines are intermingled, and again in others there are no lateral lines, all cells appearing fertile.

A histologic study of the changes following irradiation shows: a disappearance of the mother cells with continuation of the evolution of the cells of the lateral lines toward keratinization; an initial growth followed by resorption of the squamae, and temporary alterations of the stroma of the connective tissue.

A series of analogous phenomena observed in the thymus treated by roentgen rays demonstrates that the Hassell corpuscles are nonpermanent, variable formations. This suggests that the cornified pearls of non-irradiated epidermoid cancer are likewise variable, their size indicating the difference between growth and resorption. Thus the interior life of cancerous tissue is governed not only by the phenomena of growth but by the phenomena of resorption as well, the increase in the size of the tumor depending on the difference of intensity of the two phenomena. On this basis, the holocrine secretion of cancerous tissues would furnish a plausible explanation for the special properties acquired by the serum of cancer patients.—*T. Leucutia.*

GENDREAU, J. E. Far-reaching effects of gamma rays and short x-rays upon the human heart. *Ann. Surg.*, Jan., 1931, *93*, 476–480.

Different types of cancers were chosen, of different malignancy, localized or with metastases, early or well advanced and in good or bad general condition. The age incidence varied from ten to seventy-two years. The lesions were in various parts of the body, some treated by roentgen rays or radium alone and by radium and roentgen rays combined.

The tracings are compared with those taken before irradiation. The records show the action of the rays upon the heart by additional "P" waves, and impure flutter; by flattening of the "P" waves and auricular fibrillation; by abnormal Q.R.S. complexes; by deep inverted "T" waves. T. P. is generally increased and the resulting rhythm slower immediately after a treatment. Tachycardia is less common than bradycardia.—*F. K. Alexander.*

GABRIEL, GERHARD. Indications and results of grenz-ray therapy. *Klin. Wchnschr.*, 1930, *9*, 2210.

Based on a study of the literature and his own investigations, Gabriel presents in this article a compilation of known facts regarding borderline rays. He emphasizes that more energy reaches the deeper layers of the skin than assumed by Bucky if a tube potential of 9 kv. is used. The harmlessness of these rays must also be doubted since late reactions were reported, particularly following the application of high doses. The only advantage is the absence of an epilating effect in man. The author concludes that provided an exact dosage is used, these rays are as beneficial in superficial therapy as ordinary roentgen rays and may even be better in a few instances. The results obtained by Bucky following total body exposure in a number of diseases of functional nature and endocrine disturbances are also mentioned.—*E. A. Pohle.*

FREUND, LEOPOLD. Die gegenwärtigen Methoden und Erfolge der Krebsbestrahlung mit verteilten Dosen. (The present methods and results of radiation therapy of cancer using

subdivided doses.) *Strahlentherapie*, 1930, *37*, 795–797.

Freund, of Vienna, the originator of treatment of cancer with radiation therapy, using small, subdivided doses, defends his priority in this type of treatment against the French and Swiss radiologists, Coutard and Schinz. He calls attention to his early publications on this method and also cites a few cases which he treated, and in which he obtained excellent results.—*Otto Glasser.*

Treves, Norman, and Pack, George T. The development of cancer in burn scars. *Surg., Gynec. & Obst.*, Dec., 1930, *51*, 749–782.

The ulcers which occur in burn scars were first described in 1828 by Marjolin and today are known as "Marjolin's ulcer." Of the 28 cases observed by the authors at the Memorial Hospital, New York, 75 per cent were of the squamous cell type and 25 per cent were basal cell. Cancers developing acutely in recent burns occurred on an average about four months after the burn. These developed in burns occurring in older people with senile, atrophic skin. Cancer developing in a burn scar late, the chronic scar burns, occurred on an average of 32.5 years from the date of injury.

The development of cancer in lupus scars, in scars of sinuses, in scars communicating with necrotic bone as in osteomyelitis, in scars of amputation stumps, in scars of roentgen burns, in scars of animal and insect bites, in vesicovaginal fistula and fistula in ano has been observed and reported many times.

Avascular scar tissue is poorly nourished and is subject to trauma and ulceration. Trauma easily destroys the delicate epithelium. Healing after each injury is more difficult. The regenerated integument is progressively inferior and persistent stimulation to the marginal epithelium for repeated growth and repair with constant frustration may lead to a loss of tissue restraint and eventually cancer.

Radiation therapy, especially the use of heavily filtered radium at a distance, is the indicated treatment for these lesions. The authors state that local excision of well-developed scar cancer is unsuccessful and dangerous. Surgical intervention should be considered only if the cancer proves to be radioresistant.

This is a most comprehensive article.—*J. H. Vastine.*

Nurnberger, L. Roentgen mutations and late injuries from roentgen rays. *Klin. Wchnschr.*, 1930, *9*, 2233.

The author, who has done considerable research concerning the injurious effects of roentgen rays on the offspring, reviews critically in this article the recent literature on the subject. He comes to the conclusion that one can almost safely state today that there is no late injury to the offspring following roentgen exposure of the parental generative organs. The mutations which Muller and other investigators found in the fruit fly cannot be interpreted in a positive sense. The majority of their observations must be regarded as early injuries. The only experiment of Muller which might be used in favor of late injury cannot be accepted because it is not certain that it is not also an early injury. The same holds true of the experimental work of Whiting. From the investigations of Harris, Hanson, and others, it appears that the effect of irradiation of the gonads of the fruit fly ceases to affect the offspring fourteen days following the exposure.—*E. A. Pohle.*

Kleinschmidt, O. The roentgen treatment of carcinoma. *Klin. Wchnschr.*, 1930, *9*, 1875.

The author who is a surgeon presented his views concerning irradiation of malignant tumors before the meeting of his County Medical Society. He sums up his opinion as follows: The improvement of roentgen apparatus and treatment technique has not changed our standpoint that operable malignant tumors should be operated on. There are only very few exceptions to this rule. In borderline cases, it must be decided in each individual case whether operation or irradiation should be chosen. This sometimes calls for an exploratory operation. There is also the possibility that an inoperable tumor may become operable following radiation therapy. Postoperative irradiation should be carried out regardless of whether the patient underwent radical operation or only a partial operation. In some cases postoperative irradiation may not be advisable; carcinoma of the stomach is, in the author's opinion, one of them. Inoperable tumors should be irradiated with as high a dose as possible. The best of all treatment methods at present seems to be the application of a high dose in order to destroy as much of the tumor as possible. The field selector designed by Holfelder is recommended as a good tool in order to bring about homogeneous

radiation throughout the malignant tumor. We cannot state today how much our results may be improved by the so-called saturation method. —*E. A. Pohle.*

TRAUTMANN, EDGAR, and PANSDORF, HANS. Roentgen treatment of chronic encephalitis. *Klin. Wchnschr.*, 1930, *9*, 1444.

Inflammatory processes are often favorably influenced by small doses of roentgen rays (Heidenhain). The authors therefore studied the effect of roentgen therapy in cases of chronic encephalitis. Two lateral fields were used in such an angle as to obtain homogeneous irradiation of the brain with from 10 to 25 per cent S.U.D. Technique: 200 kv., 7 ma., 0.5 mm. Cu, 40 cm. focal skin distance, 8×10 cm. field of entry. After a careful study of 6 cases, the authors came to the conclusion that this treatment did not influence the disease at all. Their findings are not only important from a practical therapeutic standpoint but are also of interest to the radiobiologist. It seems that the inflammatory processes in the brain are different from those in other tissues.—*E. A. Pohle.*

HAYER, E. Roentgen therapy of toxic goiter. *Klin. Wchnschr.*, 1931, *10*, 297.

The author analyzes 152 cases of toxic goiter which were treated by roentgen rays. The dose must be carefully adapted to the needs of each individual patient. It is best to start with small doses of 60 r per area over thyroid and thymus, one field per day, followed by 14 to 20 days' interval. If this is tolerated well, then 90 to 120 r per field may be given followed by 14 to 20 days' interval. The dose is then increased to 150 to 180 r per field and repeated at the same or longer intervals. Irradiation of the hypophysis (two temporal fields, 6×8 cm., 240 r per field, 180 kv., 0.5 mm. Cu, half-value layer in copper = 1.15 mm.) has also proved of value. It seems essential, however, to administer this treatment only after the thyroid has already responded to irradiation. Basing the evaluation of the results on the objective signs, basal metabolic rate and pulse rate, it appeared that 107 cases were definitely improved while 13 cases appeared worse; 2 patients died. In 18 patients there was an improvement but no drop of the basal metabolic rate. Ten cases were improved but the pulse rate remained high. In two patients, the B.M.R. rate dropped but there was a continued high pulse rate with loss of weight. In 13 per cent of all cases, the most objective sign, namely, the B.M.R. could not be relied upon alone to judge the efficacy of the treatment. Additional therapy to the hypophysis was given in 58 cases; in 21 cases because of tachycardia, in 21 cases because of headache, in 6 cases because of vasomotor symptoms, in 9 cases because of dizziness, in 6 cases because of general irritability, in 7 cases because of insomnia, and in 2 cases because of exophthalmos. It is also stated that considerable improvement could always be noted following a prolonged stay of the patients in suitable climates. —*E. A. Pohle.*

REGAUD, CL. Fondements rationnels et indications de la radiothérapie (radium, rayons X) dans le traitement des cancers du sein. (Rational fundamentals and indications of radiotherapy (radium, roentgen rays) in the treatment of cancer of the breast.) *Arch. Inst. du Radium de l'Univ. de Paris*, *2*, 421–442.

I. The cure of cancer of the breast by means of radiation therapy is exceedingly difficult. One must draw a sharp line between the palliative results and a true cure. This latter can be estimated only after a period of ten to fifteen years.

II. Inasmuch as the epithelial cancers of the breast represent numerous clinical varieties, the histophysiologic and radiophysiologic properties of which are manifold, no definite basis can be established for the evaluation of the radiotherapeutic prognosis nor for the best method of treatment to be followed. The variation in thickness (as, for example, an ulcerated scirrhous carcinoma in a thin woman or a massive tumor in a large breast) creates conditions which further complicate the problem of irradiation. This becomes still more apparent when one considers the extensive and peculiar dissemination of the carcinoma.

III. Every cancer of the breast, therefore, must be examined and treated by a group of physicians of the various specialties (surgery, roentgen rays, radium). Small tumors in thin breasts give favorable results by juxtacutaneous curie therapy (plastic molds). Massive tumors in large breasts are best treated by diathermic amputation associated with pre- or postoperative irradiation (roentgen rays or radium). Cutaneous and subcutaneous manifestations as well as the supraclavicular glandular metastases respond well to juxtacutaneous

curie therapy while the axillary metastases, owing to the necessity of crossfiring, are irradiated more effectively with roentgen rays. Radium puncture of the primary tumor of the breast, although it appears logical, may lead to metastatic dissemination. Postoperative irradiation is indicated in all instances in which the surgical removal remains incomplete.—*T. Leucutia.*

Wood, Francis Carter. Palliative therapy of malignant growths. *Radiology*, March, 1931, *16*, 291–301.

The author estimates that 80 per cent of all persons suffering from cancer are incurable by surgery. A few of these patients may be cured, and more can have their lives prolonged over a considerable period of years by radiation. Another group can gain relief from pain and a certain amount of psychic comfort from irradiation, though there is no evidence that life is prolonged. Too much stress has hitherto been laid on the attempt at permanent cure by heavy irradiation, which too often renders the patient's life miserable or actually shortens it. —*J. D. Camp.*

Lazarus-Barlow, W. S. Experimental use of a large quantity of radium in treatment. *Ann. Surg.*, Jan., 1931, *93*, 371–379.

The author presents the results obtained in treating cancer with 2.5 grams of radium element. In this work only gamma radiation at a close distance was utilized; a period of four to five hours was considered the limit which human skin could stand although the production of a radium burn was of inferior importance to the attempt at influencing the disease beneficially.

The results of this irradiation on the blood, the gastrointestinal tract, the skin and other local phenomena were essentially the same as have been observed before from radium irradiation where smaller quantities of the element were used.

Malignant disease of the breast, tongue, neck, esophagus, rectum, lip plus other sites not as common, in addition to lymphosarcoma and leucemic conditions were treated with this large amount of radium with nothing unusual in the end-results in any of the cases.

The author concludes that there is considerable potency in a large amount of radium but raises the question as to whether the advantages outweigh the disadvantages and does not attempt to answer. He does believe that whatever beneficial effects are obtained are due to the radium as such, apart from the quantity used.—*F. K. Alexander.*

Phemister, Dallas B. Undifferentiated round-cell sarcoma. *Ann. Surg.*, Jan., 1931, *93*, 125–131.

The usual teaching in connection with malignant tumors is that the less differentiated the cell, the more malignant the tumor, the earlier it gives rise to metastases, and the worse the prognosis. This has been held particularly true for carcinoma, though the author believes that sarcoma presents exceptions to these rules oftener than carcinoma, and particularly so in the undifferentiated round-cell sarcoma frequently met with in connection with the bones and connective tissue of the soft parts of the extremities.

During the period from 1919–1925, the author had 5 such cases and all were alive and free from symptoms in July, 1930, varying from four years and eight months to ten years and nine months. Of this group 4 were entirely undifferentiated and almost entirely devoid of stroma except for blood vessels. One tumor showed organoid structure in that it possessed a connective tissue stroma in places.

It was interesting in view of the fear entertained by many of spreading metastases through operative interference, that biopsy was done in 4 cases, and that in one case there was an extensive regional excision eighteen months previously, followed by a prompt recurrence.

The treatment was varied. In one case amputation was the only method employed; in another case both radium and roentgen rays were used; in 2 cases preoperative irradiation followed by excision, implantation of radium and subsequent irradiation was the method of choice. In the one other case the tumor disappeared under roentgen irradiation, after which the bone involved was excised and further roentgen irradiation given.

The author presents in detail the case histories of the 5 patients studied.—*F. K. Alexander.*

Lambranzi, Mario. Sulla roentgenterapia del fibroma rino-faringeo. (On the roentgen therapy of a rhinopharyngeal fibroma.) *Arch. di radiol.*, Jan.–Feb., 1931, *7*, 62–68.

A case of rhinopharyngeal fibroma occurring in a boy nine years of age which responded favorably to roentgen therapy is briefly described. The following was the therapeutic procedure: January 18, 1930: first series consisting of two fields (one on each side), 0.5 mm. Cu plus 3 mm. Al filters, 6×8 cm. field, 28 cm. skin target distance, 2 ma., 37 cm. spark gap, 20 minutes, 60 per cent S.U.D. on the surface. Three further series were administered at intervals of one month, except the last which was given at intervals of two months, the technique being identical. A complete disappearance of the tumor with clinical healing was obtained.—*T. Leucutia.*

DENIER. Traitement du rhume des foins par la radiothérapie. (Treatment of hay fever by radiotherapy.) *Bull. et mém. Soc. de radiol. méd. de France*, April, 1931, *19*, 179.

Several cases of hay fever, some of them showing regular seasonal recurrences for a number of years, have been treated by roentgen therapy with excellent results. The treatment was directed to the nose (the central ray falling in the line of the pituitary gland), the following technique being used: 5×8 cm. field, 25 cm. spark gap, 8 mm. Al filter, 2 exposures of 500 R at eight day intervals. In several instances one single irradiation was sufficient to bring about complete relief.—*T. Leucutia.*

ZIMMERN, A., and BRUNET, R. Un nouveau cas de gangrène artéritique chez un diabétique traité par l'irradiation de la région surrénale. (A new case of arthritic gangrene in a diabetic treated by irradiation of the suprarenal region.) *Bull. et mém. Soc. de radiol. méd. de France*, Jan., 1931, *19*, 28–30.

An additional case of diabetic gangrene of the foot which responded favorably to roentgen irradiation of the suprarenals is briefly reported. The gangrene involved the end of the left great toe (the right leg was previously amputated) and produced an ulceration with sphacelation. The irradiation was administered in series of 4 seances given on alternate days over both suprarenals (400 R per side and per seance, 18 cm. spark gap, 5 mm. Al). The series was repeated at intervals of from two to six weeks (a total of five series). Immediately following the first series there was improvement, a complete healing with cicatrization resulting within four months.

It appears that irradiation with small fractional doses constitutes the best method of treatment.—*T. Leucutia.*

DENIER. Guérison d'un lymphangiome récidivant par la radiothérapie de la rate. (Cure of recurrent lymphangioma by radiotherapy of the spleen.) *Bull. et mém. Soc. de radiol. méd. de France*, April, 1931, *19*, 177–178.

This is a very brief case report, illustrated with photographs before and after treatment, of a case of lymphangioma at the level of the eighth rib in the left anterior axillary line, which recurred following two surgical removals and which failed to respond to radiation therapy applied locally. Later, two roentgen exposures over the spleen and one over the femur and sternum, with doses of 600 R, caused disappearance of the tumor within fifteen days. It must also be mentioned that previous to the irradiation of the spleen there was an abnormal blood picture (white blood cells, 14,000; red blood cells, 3,700,000) which later also returned to normal. The case was treated only recently and therefore no opinion can be expressed as to the final outcome.—*T. Leucutia.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

A. U. DESJARDINS

MAYO CLINIC

ROCHESTER, MINNESOTA

SECTION TWO

CONTENTS

(*Current Number, February, 1932*)

Animal Experiments (continued) 25

Analysis of Experimental Data 44

(*To be Continued in the March, 1932, issue*)

(*Contents Published in the January, 1932, issue*)

PREFACE

HEART 1

General Considerations 1

Animal Experiments 1

PREVIOUSLY PUBLISHED

Action of Roentgen Rays and Radium on the Gastrointestinal Tract

July, August and September, 1931

Action of Roentgen Rays and Radium on the Eye and Ear

October, November and December, 1931

ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

Animal Experiments *(Continued)*

Radium. MAASS (1911) investigated the action of radium emanation on the isolated heart of the frog[49] by perfusing the organ with normal Ringer's solution and with Ringer's solution charged with radium emanation. This was done by means of a perfusion apparatus constructed on the principle of Jacobi, and the heart was permitted to function under circumstances approximating physiologic conditions. Variations in volume of the heart were recorded by a plethysmograph, by the rise of a column of water with varying resistances, by the excursions of a mercury manometer, and by the quantity of fluid ejected by the heart in unit time. Some experiments were conducted by artificially perfusing the heart suspended according to the Engelmann method. Perfusion of the heart with Ringer's solution containing radium emanation was reported as causing a stronger diastole, which increased to the point of diastolic standstill. The number of contractions per minute diminished 50 per cent, and the minute volume also decreased. This was often accompanied by irregularities, such as alternating rhythm and dicrotism of the atrial pulse. These effects could be made to disappear and normal cardiac function could be restored by perfusing the heart with plain Ringer's solution. Weak concentrations of radium emanation sometimes caused an increase in cardiac activity, and this was regarded as stimulation of the organ by the radioactive substance.

TSIWIDIS (1912), influenced by the experiments of Plesch and the clinical observations of F. Frans, investigated the influence of intravenous injections of thorium X on the blood pressure of adult rabbits. The pressure and pulse were determined by means of a Gad-Cowl tonometer and a kymograph. It was first found that, after the injection of large doses of thorium X (125,000 and 250,000 Mache units per kilogram) into the ear vein of the rabbit, the blood pressure diminished for a short time, then rose abnormally, and later returned to normal; the pulse rate also diminished and the amplitude of the pulse increased. The effect of different large doses of thorium X was then studied with the electrocardiograph. In some of the experiments the negative pole was connected to an electrode passed into the esophagus, and the positive pole to another electrode introduced through the anus. Electrocardiograms were made before and at varying intervals after the injection. These experiments showed that large and small doses were followed by a distinct bradycardia and changes in the height of the waves. The bradycardia was most pronounced after strong doses and at the end of the experiment and consisted in lengthening of the interval between two cardiac phases and of the section of the curve given by the sum of these waves. The A/P wave (Einthoven) was most influenced at the beginning of the experiment and directly after the injection. Later the wave decreased and this decrease was maintained to the end. According to the number of Mache units of thorium X injected, the initial variation in the I wave diminished absolutely and relatively and did not return to normal for at least an hour. The negative variation in the Ip wave resembled that of the J waves. The F wave or the final deviation was not affected by small doses; after doses of 70,000, 85,000, 110,000, and 250,000 Mache units, respectively, per kilogram of body weight, this wave showed a tendency to enlarge; in one experiment with 500,000 Mache units per kilogram the wave diminished. The increase in the size of this wave was thought to correspond to an increase in the strength of the heart.

MAASS and PLESCH (1913) tried to ascertain whether or not thorium X had the same effect on the heart as Maass (1911) had found with radium emanation. These experiments also were conducted on the isolated heart of an uncertain number of frogs, and the method

[49] No mention was made of the number of frogs or the quantity of radioactive substance, and the results were given only in general terms.

Journal Page 305

was essentially the same as in the earlier experiments of Maass. The principle involved was that the heart was filled with Ringer's solution under the slightly excessive pressure of approximately 30 millimeters of water, which entered through the upper left vena cava, traversed the heart, and passed out through a cannula introduced into the left aorta. The resistance to the vascular system could be varied by means of a capillary tube fixed to a cog wheel, which could be immersed to varying depths in a test tube, with lateral overflow, filled with mercury to within a few millimeters below the overflow. The blood from the heart dropped from the overflow and was measured by a Jacobi current measure, each filling and emptying being indicated on a kymograph by means of an electro-magnetic recorder. A registering mercury manometer in the overflow and a water tube to read the height of the column of water coming from the heart also were provided. The plethysmographic curve of the heart was obtained in a closed glass vessel, through the cork of which passed the afferent and efferent cannulae and a free-ending glass tube connected to a Maass volume indicator. The resistance was such that the heart made good, uniform contractions and ejected sufficient amounts of fluid. The nutrient fluid was a Ringer's solution with a viscosity approximating that of frog serum, but the arabic acid was replaced by ordinary gum arabic, part of the salt content of which had been removed by soaking in repeated changes of fresh, cold water. The amount of gum was 35 grams per liter.

A dose of radioactivity of 40 electrostatic units per cubic centimeter caused the arterial pressure to diminish one-half and the minute volume to one-ninth of the original value, indicating a marked decrease in the activity of the heart. This was accompanied by a slight increase in rate. This effect was transient, however, and great improvement followed perfusion with plain Ringer's solution. The same reaction followed each repetition of the test, but this was never so pronounced as in the first instance, probably because the heart did not recover its full function after the first exposure to the radioactive substance. Doses of 10 and 4 electrostatic units yielded the same qualitative results. Doses of 0.4 electrostatic units caused only a slight decrease in minute volume and function. In another experiment, in which the inflow pressure against which the heart must work had been reduced to 30 millimeters of water, the addition of 0.218 electrostatic units of radioactive substance caused an increase in cardiac activity evidenced by a great increase in the minute and pulse volumes. A dose of 2.18 electrostatic units was followed by augmentation in the minute and pulse volumes, accompanied by a slight decrease in rate. With 21.8 electrostatic units both the minute volume and frequency diminished, while the pulse volume became abnormally high. The results of a third experiment, in which doses of 8.3 and 110 electrostatic units were given, were the same as in the first experiment. Large doses had less effect than small ones. Experiments with Engelmann's suspension method[50] showed that large doses of thorium X diminished the excursion of the auricle, while the excursion of the ventricle increased.

Direct plethysmographic study[51] of the heart of cold blooded animals, with intravenous injection of from 100 to 1000 electrostatic units of radioactivity, caused the middle segment of the heart to be displaced toward the side of diastole. The heart, which at the outset beat freely in the small funnel, filled the funnel completely after the administration of thorium. The number of the contractions diminished, but their force increased. One frog heart, which had been injured by perfusion of 10 electrostatic units of thorium X but whose excursions were still good, though the volume of outflow was small, was exposed to more radioactivity by allowing the solution containing the thorium X to flow directly into the heart (small negative pressure). This was followed by greater diastolic distention, and Maass and Plesch thus explained the individual variation in the curves obtained. Intravenous injection of 1,100

[50] The material was injected directly into the veins of the abdominal wall.

[51] A small opening having been made in the pericardium through the usual "cardiac window," a small bell-funnel, covered with vaseline, was pushed between the pericardium and the heart and was held in place by the elasticity of the tissues. A small frog-heart plethysmograph was connected to a Maass volume indicator by a heavy rubber tube.

electrostatic units led to a distinct increase in ventricular work indicated by a greater amplitude, a change in the form of the pulse, and an increase in the activity of the auricle. After doses of 3,000 electrostatic units, the arteries became arrhythmic, while the ventricle performed normally, though slowly. Maass and Plesch interpreted these results as an indication that thorium X and radium emanation increase the diastolic distensibility of the heart, and concluded that thorium X improves cardiac activity and lowers the vascular resistance.

Further experiments were undertaken to test the influence of thorium X on blood pressure. A rabbit, into which 1,500 electrostatic units of this radioactive substance had been injected, remained alive, but its weight diminished as much as 33 per cent for a time. Another rabbit, which had received only 600 electrostatic units, died in eight days. At necropsy, hemorrhages were found in the gastrointestinal mucosa, kidneys, and fasciae. Similarly, one guinea pig, into which 1,000 electrostatic units of thorium X had been injected, became severely prostrated within one-half hour, but survived; while another, which had received a smaller dose with no apparent immediate effect, died within ten days from pronounced intoxication. Injection of 3,000 electrostatic units into one cat was followed by a distinct rise in the blood pressure, but the additional injection of 9,300 electrostatic units had no further effect. Such variable results made Maass and Plesch hesitate to draw conclusions. Nevertheless, basing themselves on the experiments of Plesch and Karczag on man, which had shown an apparent drop in blood pressure and diminution in pulse rate, Maass and Plesch tried to ascertain if thorium X could influence blood pressure by acting on the vagus. Without describing these experiments, they expressed the opinion that thorium X diminishes the sensitiveness of the cardio-inhibitory fibers of the vagus or of the nerve endings.

Prime (1916) studied the action of radium on the heart muscle of a large number of chick embryos.[52] The heart was removed from chicks incubated for seven days, cut into pieces about 0.005 gm. in size, suspended in a hanging drop of Ringer's solution, and sealed over a deep slide. Twenty-five bits of such tissue were placed in each drop. One of these preparations was kept as a control, while the others were covered with 0.4 millimeters of brass[53] and exposed to 0.100 gm. of radium for one-half and two hours, respectively. Each piece of tissue was then removed and planted in slightly diluted chicken plasma, to which an extract of whole chick embryo was added, and the preparations were kept in an incubator at 37°C. Daily observations were made, and after from forty-eight to seventy-two hours, the pieces of tissue were removed from the plasma, washed in warm Ringer's solution, and replanted in fresh plasma and extract. At the end of twenty-four hours, all the irradiated and unirradiated (control) explants were found to be growing profusely, and active contraction of the muscle was noted in all cases. Often it seemed as if the tissues exposed to radium for a short time grew more profusely than the controls, but the constancy of this impression was not verified. After forty-eight hours growth had proceeded further, but the pulsations were less active.

The tissues were then washed and transplanted, and the second generation was studied after twenty-four hours. No great difference between the irradiated and unirradiated (control) preparations was noted; all the cultures grew well. However, the number of pulsating fragments of tissue was usually smaller than in the original cultures. These were transplanted again at the end of forty-eight hours and, when this third generation was examined twenty-four hours later, a marked difference was perceived. The controls and the preparations exposed to sublethal doses of radium continued to grow, but marked inhibition of growth was found in the cultures irradiated for two hours. Slight growth was perceptible in one or two specimens, but a vast majority had ceased to grow altogether, though the persistent beat of many proved them still alive. The explants of the fourth generation did not grow after a large dose of radium, but some fragments of tissue continued to pulsate. Moreover, a smaller

[52] The number of hearts used was not mentioned.

[53] Such filtration allowed much of the beta and gamma radiation to pass through and to act on the tissue.

number of the cultures of this generation, which had been exposed to a small dose of radium, continued to grow, and such growth was less vigorous than in the controls; but, in spite of this, many of the explants which failed to grow continued to beat. Practically no growth was found in any of the cultures of the fifth generation, though many were still beating, whereas the controls grew and contracted normally. No change was seen between the fifth and the ninth generations. These results werer egarded as substantiating Hertwig's view that radium acts chiefly on the nuclear mechanism of cell division and not on the protoplasm.

Feenstra (1916) found that the heart of frogs,[54] prepared for perfusion by being placed on a cannula and perfused with Ringer's solution[55] devoid of potassium chloride, soon ceased to beat, although the time required for this reaction varied with the individual heart. On subsequent addition of potassium chloride, the heart began to pulsate spontaneously and regularly. Uranium compounds instead of potassium were next tested. After the cardiac contractions had stopped as the result of perfusion with potassium-free Ringer's solution, 0.025 milligrams of uranium nitrate ($U(NO_3)_4$) was added to the solution, and after perfusion for about five minutes spontaneous and regular cardiac contraction was resumed. This was repeated successfully sixteen times. On discontinuing the uranium-Ringer's solution and perfusing with normal Ringer's solution, the heart instantly ceased to contract in diastole, and this could be relieved only by using Ringer's solution devoid of potassium or a solution containing uranium. If, after coming to a standstill, the heart again began to pulsate, the pulsations, electrocardiogram, and tonus were normal. If the initial perfusion with potassium-free Ringer's solution was not sufficient and cardiac contraction ceased from potassium insufficiency, the heart did not recover its power of contraction when subsequently perfused with Ringer's solution devoid of potassium, with solution containing uranium, or with ordinary Ringer's solution. Prolonged perfusion with Ringer's solution containing uranium, but not potassium, caused the heart to recover. In three instances the heart, which did not beat at the beginning when perfused with solution containing potassium, resumed pulsation when perfused with potassium-free solution containing uranium; and impurities could not be held responsible. Excessive quantities of uranium had a toxic action, but this could be neutralized by adding $CaCl_2$, providing the proportions were maintained.

Feenstra (1916) continued his studies by using a solution of uranium at 18°C., prepared with Ringer's solution free from potassium, to each liter of which 50 milligrams of thorium nitrate were added. The addition of too much thorium nitrate made the solution cardiotoxic, and since thorium nitrate is slowly precipitated as thorium oxide, it was necessary to use a fresh solution. First the heart of the frog[56] was perfused for fifteen minutes with normal Ringer's solution, then with Ringer's solution free from potassium, and finally with solution containing thorium nitrate. The heart, which ceased to pulsate during perfusion with potassium-free Ringer's solution, again began to beat spontaneously and regularly when the solution containing thorium nitrate was used. Thirteen tests gave contractions normal in size and frequency; the electrocardiogram also was normal. Tests for impurities of potassium or rubidium were negative. The toxic action of thorium nitrate could be neutralized by increasing the quantity of $CaCl_2$, when the cardiac reaction was normal.

Zwaardemaker (and Feenstra) (1916),[57] on the assumption that potassium is the only radioactive element normally present in the animal organism, undertook to ascertain the effect on the heart of frogs of replacing potassium by other radioactive elements in non-toxic doses. The dosage of these elements in physiologic salt solution was estimated from the radioactive (total radioactivity), and not from the molecular, standpoint. With potassium, rubidium, uranium, and thorium, the heart continued to beat for hours in the perfusing fluid,

[54] Number of frogs and controls not stated.
[55] Distilled water, 1000.0; sodium chloride, 7.0; calcium chloride, 0.2; sodium bicarbonate, 0.2; glucose, 1.0.
[56] Number of frogs not stated.
[57] Feenstra conducted the experiments at the suggestion of Zwaardemaker.

precisely as if plain Ringer's solution had been used. Comparative tests of the salts of radioactive elements gave similar results, which appeared to be related to the conduction mechanism of the heart, because the electrocardiograms corroborated the myograms and the reactions were reversible. The frog heart, isolated from the body, was perfused with normal Ringer's solution[58] for fifteen minutes to give the organ an opportunity to recover. The Ringer's solution was then replaced by solution free from potassium; this was followed by slowing and irregularity of the heart beat and, soon afterward, by complete cessation of cardiac activity. The heart was then immediately perfused with potassium-free Ringer's solution, to which 7 cubic centimeters of radium bromide solution, corresponding to about 3 micrograms,[59] was added after neutralization. In ten such tests, perfusion with radioactivated Ringer's solution free from potassium was invariably followed by a return of cardiac pulsation. At first the contractions were irregular, but the rhythm soon became as regular as during perfusion with normal Ringer's solution. Changing from the radioactive solution to potassium-free solution without radium again brought the cardiac function to a standstill, but only after the heart had continued to beat for one hour. The cardiac impulse returned within from three to ten minutes after resuming perfusion with the potassium-free solution containing radium. When this was followed by perfusion with normal Ringer's solution, the heart stopped beating immediately and did not recover until one hour later. This was held to agree with the results obtained previously with uranium and thorium, and to indicate a summation of the possible diffusing ions and the rapidly penetrating potassium ions. The radium solution and the reagents were tested for potassium. A liter of each of the potassium-free and radium solution contained less than 2.5 mg.—a quantity of potassium regarded as insufficient to maintain the cardiac impulse. In another series of experiments the emanation in the radium solution used to prepare the perfusion fluid was withdrawn by boiling and the solution neutralized; but again suitable doses caused the heart, whose activity had previously ceased, to resume regular pulsation. Zwaardemaker deduced that potassium, rubidium, uranium, thorium, and radium in suitable doses have the same effect on cardiac activity. No conclusions were drawn, but the implication was that the regulatory or other influence of potassium on the heart is due to its radioactivity.

Fromme (1916) tested the influence of radium on the heart of two frogs by making, under aseptic conditions and slight chloroform anesthesia, an incision on one side and parallel to the spinal column, above the pelvis, and by placing in the muscles of the back and suturing in position a capsule[60] containing 24 milligrams of mesothorium. The capsule was removed after fifty hours, and twenty-three days later the animal was killed by decapitation and placed at once in 4 per cent formalin. Microscopic inspection of frozen sections stained with Sudan III showed fatty degeneration of the cardiac muscle. In the second frog the same capsule of mesothorium was similarly placed under the skin between the eyes, and was removed after twenty hours. This frog died spontaneously five days later, and frozen sections of the various organs, hardened in formol and stained with Sudan III, showed even more extensive fatty degeneration of the heart muscle than in the first animal. This was attributed to closer proximity of the radioactive source.

An axolotl was placed in an Erlenmeyer flask approximately 6 centimeters high, filled with aquarium water to a height of 2 cm., and a silver tube[61] containing 50 milligrams of radium was added.[62] The radium tube was removed after fifteen hours, and the pulse rate, which before irradiation had been 60, had diminished to 40 at the end of fifteen hours, to 35 two hours later, to 16 four hours later, and death ensued six hours after irradiation. Fatty degeneration of the heart was noted. Another axolotl irradiated in the same manner, with

[58] NaCl 0.7 per cent; KCl 0.01 per cent; $CaCl_2$ 0.02 per cent; $NaHCO_3$ 0.02 per cent; glucose 0.1 per cent.
[59] One liter of the solution of radium bromide contained 1000 Mache units.
[60] The character of the capsule was not described.
[61] The thickness of the silver tube was not specified.
[62] The distance between the axolotl and the radium was not mentioned.

radium filtered through lead, lived for thirty days. Progressive slowing of the pulse rate again was found. One mouse was exposed to filtered roentgen rays[63] for fifteen minutes and to unfiltered roentgen rays for forty-five additional minutes on the same day. The animal was immediately killed by decapitation and the organs hardened in 4 per cent formalin. The heart was found to contain much fat. Fromme concluded that the outstanding effect of irradiation of the heart of cold and warm-blooded animals is fatty degeneration.

Zwaardemaker, Benjamin, and Feenstra (1916), basing themselves on the conclusions drawn by Zwaardemaker from his experiments with Feenstra (1916) that the reactivating influence of potassium on the heart of frogs was due to the radioactivity of this element, tried to ascertain the effect on cardiac function of the beta and gamma rays of radium. One capsule[64] containing a quantity of mesothorium equivalent to 6 milligrams of radium bromide, and a second capsule[64] containing 3 milligrams of radium bromide, were used. Frogs[65] of moderate size were killed by destruction of the central nervous system, the heart was exposed, and a Kronecker perfusion cannula was introduced into the inferior vena cava, where the cannula was secured by means of a ligature looped around the auricle, half-way between the sinus and the ventricle. As soon as normal Ringer's solution had caused the cardiac pulsations to become regular, Ringer's solution free from potassium was made to perfuse the heart at a water pressure of 9 centimeters. In from one to sixty minutes (average, 30 minutes) the heart ceased to beat. The radioactive capsule was then brought to between 0.25 and 2.0 centimeters from the organ. This had no immediate effect, but after from one to sixty minutes with mesothorium, and from one to eighty-two minutes with radium bromide (average, 24 and 27 minutes, respectively), the heart again began to pulsate. At the outset, the pulsations were stronger with the mesothorium than with the radium bromide preparation. On withdrawing the radioactive substance, the cardiac pulsations diminished and ceased after a lapse of from one to fifty-five minutes (average, 25 minutes). From this it was deduced that the heart may stop beating from lack or from excess of radioactivity and that these two kinds of arrest may be distinguished by simply stopping the flow of Ringer's solution free from potassium through the irradiated and pulsating heart and to perfuse the organ with normal Ringer's solution. In the event of excessive radioactivity the change from potassium-free to normal Ringer's solution is followed by immediate cessation of the heart beat. In the event of insufficient radioactivity the heart beat suddenly increases and continues indefinitely. This paradoxical phenomenon may be repeated several times in the same heart.

The action of mesothorium at a distance of 1 centimeter was too strong, while that of radium was too weak; this may have been due to a difference in distribution of the radioactive substance in the two capsules. The mesothorium was concentrated into a small ball, while the radium bromide was spread over a surface about one-third of a cubic millimeter. It was assumed that the beta rays penetrated the nearest half of the heart more rapidly than the remote half, while the gamma rays penetrated the entire organ more evenly. The part of the organ nearest to the radioactive preparation must, therefore, have been exposed more than other parts. To these factors, as well as to variation of individual hearts, were attributed the differences in reaction time. Thirty-four such tests were made without a single failure. In two instances the heart beat, revived by irradiation, was abnormal in character; this occurred in hearts with exaggerated tone; in all the other tests the beats were full and regular. Only contractions of the entire ventricle were noted; the movements of the auricle were disregarded. The number and strength of the contractions were increased by the addition of 100 mg. of non-toxic fluorescin per liter of solution. This increased the effect, not only of perfusion with radioactive salt but also of irradiation. Perfusion with Ringer's

[63] Müller boiling-water tube; focal-skin distance, 21 cm.; 3 to 3.5 ma.; quality, Wehnelt 11; filter not mentioned.
[64] The character, shape, and thickness of the capsule was not specified.
[65] The number of frogs was not mentioned.

solution free from potassium sometimes induced independent groups of contractions, but never an uninterrupted succession of pulsations. Ringer's solution free from calcium also caused a rapid cessation of the heart beat, and in one instance the cardiac impulse was not restored by irradiation, in contrast to the usual sequence of events. Exposure to radium for one-half, one, or one and one-half hours, at a distance of 0.5 cm., of the heart of a frog, of which the pulsations had been arrested by perfusion with calcium-free Ringer's solution, caused the organ to resume its rhythmic contraction as soon as it was perfused with potassium-free solution, but not after exposure to normal Ringer's solution. Moreover, changing from solution devoid of potassium to normal solution after contraction had been initiated by the former brought the heart to an instant stop. This was ascribed to residual secondary radioactivity sensitized by fluorescin. Besides the antagonistic action of radium on the heart, arrested through lack of potassium, Zwaardemaker, Benjamins, and Feenstra also drew attention to the frequent absence of mechanical irritability in hearts, the contractility of which had been abolished by perfusion with Ringer's solution free from potassium.

ZWAARDEMAKER (1916–1917) sought to determine the quantitative relations between the effect of 5 mg. of mesothorium in a glass capsule placed at different distances, 40 mg. of potassium chloride, and 10 mg. of uranyl nitrate per liter of solution, to which the neutralizing quantity of uranyl salt was added for each distance. A frog heart, prepared according to the method of Kronecker, was perfused first with normal Ringer's solution and later with solution free from potassium.[66] At a certain moment this inactive solution was replaced by a similar solution, to which 0.040 gm. KCl and 0.010 gm. of uranyl nitrate had been added, but the heart remained quiescent. When the glass capsule containing 0.005 gm. of mesothorium was placed at a distance of 8, 7, 6, 5, 4, 3, 2, and 1 mm. respectively, the heart began to beat after from one to sixty minutes (average, 13 minutes). As soon as this occurred, an excess of uranyl nitrate was added to the perfusing fluid.[67] This was continued until the cardiac contraction ceased, but mechanical stimulation induced contraction. Such arrest of cardiac activity could be maintained for from five to ten minutes. The relation between irradiation and excess of uranium in the perfusing fluid was as follows:

Distance between mesothorium and heart (in millimeters)	Uranyl nitrate added to original solution (in milligrams)
8	2
6	5.5
5	7
4	8
3	12
2	20
1.5	30
1	40

This knowledge made it possible to duplicate the effect several times by varying the distance of the mesothorium or the quantity of the uranium salt. Alpha rays were not thought to play a part in this effect on the heart, which occurred even when the rays were filtered through 0.2 mm. of aluminium. As shown by a small ionization chamber, the beta rays were partly absorbed by the heart, while the gamma rays were not absorbed. The biologic effect of the beta rays was further shown by the fact that the quantity neutralizable by uranium became inactive at a distance of 9.5 mm., while at 6 mm. a quantity equivalent to an excess of uranyl nitrate of 0.005 gm. per liter was present. The return of pulsation after perfusion with potassium-free Ringer's solution or with a solution containing exactly balancing

[66] The solution contained 7.0 NaCl.; 0.200 $CaCl_2$, and 0.200 $NaHCO_3$ per liter.
[67] This was done by adding a solution containing 0.001 gm. of the salt per c.c.

amounts of potassium and uranium was, therefore, attributed to weak beta rays, which were absorbed according to an almost exponential law. The fact was stressed that the quantity of uranium which neutralized the effect of irradiation at different distances, so that the heart stimulated to pulsation by mesothorium again ceased to beat, was subjected to the same quantitative value as the absorbed radiation. This quantitative relationship was held to support the assumption that the biologically effective quantity of energy furnished by the weak beta rays and the dose of uranium necessary to establish an equilibrium and to arrest cardiac activity are antagonistic. Similar tests with a preparation containing 3 mg. of radium yielded the following equilibrium data:

Distance between radium and heart (in millimeters)	Uranyl nitrate added to original solution (in milligrams)
4.0	5.0
3.5	6.5
3.0	9.0
2.5	11.5
2.0	15.0
1.5	18.0
1.0	22.0

Zwaardemaker (1917), proceeding from the basis of an antagonistic relation between irradiation and uranium, undertook to study the problem further by using the automatic action of the heart as an indicator. Each heart[68] was first perfused for a few minutes with Ringer's solution free from potassium in order to remove the circulating potassium from the cells. The solution contained 7 mg. NaCl (potassium-free), 0.200 gm. $CaCl_2$ (potassium-free), and 0.200 gm. $NaHCO_3$ (potassium-free) in one liter of water. The perfusion was continued until the normal Ringer's solution used at the outset had presumably been removed from the lacunae of the heart. Then, instead of this inactive solution, one containing 0.040 gm. KCl and 0.010 gm. of uranium nitrate (including water of crystallization) was employed. The heart stopped beating in almost the same manner as when perfused with potassium-free Ringer's solution. The heart was then exposed to 5 mg. of mesothorium in a small glass tube[69] or to 3 mg. of radium bromide in a flat capsule[70] with a mica window. The mesothorium container was placed at distances of from 1 to 8 mm., and the capsule of radium bromide at a distance of from 1 to 4.5 mm. The cardiac pulsations soon reappeared. The amount of uranium in the fluid was then increased by adding a suitable uranium solution to the contents of the perfusion flask. When a certain titer had been attained, the heart beat again stopped. Arrest of pulsation for from five to ten minutes was assumed to indicate that an equilibrium between the antagonistic factors had been obtained. This was repeated two or three times in one experiment, with the same result. A definite and apparently exponential relation between the distance and the quantity of uranium, and a remarkable agreement with the laws of absorption for heterogeneous, soft beta radiation were deduced. Zwaardemaker regarded the foregoing relationship as sufficiently explicit to serve as a means of measuring the biologic action on the heart not only of radioactive, but also of chemical, substances.

Kemen and Kisch (1919) studied the effect of radium emanation on the heart of a number of *Rana temporaria*[71] weighing from 40 gm. to 80 gm. Part of the experiments were done on the excised heart and part on the organ *in situ;* the suspension method was sometimes used to obtain a graphic delineation of the activity of the auricle and ventricle. In the

[68] Presumably the heart of the frog; the number of such preparations was not mentioned.
[69] The thickness of the glass was not specified.
[70] The composition and thickness of the capsule were not given.
[71] Probably fourteen frogs.

preparation studied *in situ*, a cannula was introduced into, and attached, to the posterior vena cava at the point where the branches from the liver unite. This cannula was connected to two Mariotte flasks by a three-way cock, allowing the contents to flow toward the heart at a water pressure of between 5 and 10 centimeters.[72] Both aortas were opened so that the heart was perfused with the solution without noticeable pressure. The same method was used in dealing with the excised heart, which was then separated from the body hanging on the cannula fastened to the vein. Sakai's modification of Gothlin's solution[73] was used as the normal perfusion fluid. The nutritive solutions containing radium emanation were prepared by placing 100 c.c. of Sakai solution and radium bromide in the apparatus of E. Neumann; this yielded, in twenty-four hours, about 20,000 Mache units of radium emanation. In one Mariotte flask was placed solution free from emanation and in another flask the same solution containing varying amounts of emanation. A turn of the three-way cock sufficed to change from one solution to the other. The emanation was measured with the Engler-Sieveking apparatus. To thoroughly mix the emanation fluid and the nutritive solution, a sufficient number of glass pearls were added to 100 c.c. of fluid to completely fill a funnel of slightly more than 100 c.c. capacity. After adding the proper amount of both fluids, and taking care to avoid air bubbles, the fluids were thoroughly mixed by means of the glass pearls.

Kemen and Kisch called attention to the "extraordinarily large" doses of radium emanation used in their experiments in comparison with those employed in treating human beings. The nutritive solution contained from 10,000 to 20,000 Mache units of emanation per hundred cubic centimeters or from 100,000 to 200,000 per liter. In each experiment the radium emanation was given either in a single dose of approximately 20,000 Mache units or the same total quantity was divided into several doses and given at intervals, with repeated perfusion with normal nutritive solution. The frog heart received, therefore, from 500 to 1000 times the concentration of emanation used in treating human beings. Moreover, the dose of emanation in the experimental preparations was given, either continuously or interruptedly, within one-half hour, while in human beings the emanation acts over a much longer time and, in spite of the much smaller doses employed in the latter, perceptible changes may be produced.

In most of the fourteen experiments no effect on cardiac function was noted, but in a few instances perfusion of the heart with nutritive solution containing radium emanation appeared to produce an initial acceleration followed later by a slight depression of cardiac activity, which returned to normal after perfusion with solution free from emanation. Arrhythmia occurred in two cases; in one case this disappeared quickly after the emanation solution was stopped and the heart was perfused with emanation-free solution. Similar disturbances of rhythm were observed in one case, however, before the heart had been subjected to the action of emanation solution, and in this instance the arrhythmia disappeared while the heart was being perfused with the emanation-containing fluid. Kemen and Kisch were, therefore, unable to draw any conclusions except that doses of radium emanation such as are used in treating human beings probably do not exert an injurious action on the heart.

Zondek (1921) tried to determine the action of radiant energy on the normal heart by exposing the organ to doses of 100, 200, 300, 400, etc., up to 15,000 Mache units of radium emanation,[74] but he found that such irradiation had no influence on the heart. The same was true for uranyl nitrate, strong concentrations of which could not be used because of the injurious effect of the uranium ion itself. Zondek was led to contend that the quantity of alpha rays in 15,000 Mache units of radium emanation cannot be compared with the quantity of beta rays emanating from potassium, and consequently, that Zwaardemaker's hypothesis rests on unsubstantial grounds. He contended further that the diastolic standstill of the

[72] Pressure constant in each experiment.

[73] 6.0 gm. NaCl.; 0.1 gm. KCl; 0.065 gm. CaCl; 1.0 gm. $NaHCO_3$; 2.85 gm. of grape sugar in a liter of distilled water.

[74] A more detailed description of the experiments was not given.

heart, noted by Zwaardemaker after withdrawal of potassium, is not a permanent condition, and that periods of arrest alternate with periods of rhythmic contraction. Zondek therefore repeated Zwaardemaker's experiments, using doses of 10, 20, 25, 30, 50, 100, and 200 milligrams of uranyl nitrate, and 50, 100, 200, 300, 500, 1000, 2000, 10,000 and 15,000 Mache units of radium emanation, per liter of potassium-free Ringer's solution. Several experiments were made with each concentration. He found that the diastolic standstill resulting from the withdrawal of potassium could never be influenced by the doses of radioactive substance specified. The interrupted rhythmic pulsation of the heart sometimes returned, but this also occurred in some of the controls. In most cases the diastolic arrest of the heart finally passed over into a systolic arrest. Further experiments were conducted on the assumption that, if potassium can be replaced by radioactive substances, the increase in tone of the ventricle from withdrawal of potassium and the ensuing systolic arrest should be interfered with if both factors were made to act on the heart at the same time. In a large series of such experiments the heart was perfused with potassium-free Ringer's solution containing different concentrations of uranium or radium emanation. The results were completely negative. The increase in ventricular tone could not be excluded and the systolic arrest could not be altered as to time of appearance. Zondek concluded that his results contradicted those of Zwaardemaker and his pupils at every point; also that the action of potassium on the heart has nothing to do with radioactivity.

Lazarus-Barlow (1922) irradiated the entire body of twenty frogs, twenty-eight rats, fifteen rabbits, and nine cats with 5 grams of hydrated radium bromide. A description of these experiments will be found elsewhere (see Gastrointestinal Tract). No symptoms of any kind were noted in the majority of animals, but the rabbits allowed to survive after exposure for forty-eight hours became somnolent and, in one instance, hemorrhage from the ears occurred. Loss of weight was noted in six out of seven animals. In two animals an initial loss of weight was made up during the second week after exposure. There was no evidence of diarrhea, but after prolonged exposure there was impaired intestinal action. In the cats no symptoms appeared for one or two days after exposure, but soon or long after this, according to the duration of irradiation, the animal refused food and became somnolent. Mucus sometimes exuded from the mouth or anus, and diarrhea occurred in some cases. After short exposures, the gastrointestinal tract was distended by liquid contents mixed with gas. The lungs were mottled, contained areas of consolidation, foci of inspissated mucus, or regions of collapse interspersed with compensatory emphysema. The small size of the spleen was always noticeable. Hemorrhages were not present. After prolonged exposures, petechial or more extensive hemorrhages occurred in the muscles, the mucous membrane of the stomach, bladder, lymph nodes, sex glands, and bone marrow. The gastrointestinal tract was greatly distended and contained large amounts of mucus often mixed with blood. Extensive degenerative changes were noted in the leucocytes, especially the lymphocytes, in the circulating blood, spleen, lymph nodes, intestinal lymph follicles, and bone marrow, in the testis or ovary, the stomach and intestine, kidneys, liver, lungs, and other organs. So far as the heart was concerned, the striation of the muscle fibers was not affected by short exposures, but disappeared more and more as the duration of exposure increased. The contractile material was finely granular and fibrillated, hyaline or translucent, or vacuolated and fragmented, as the irradiation or survival was prolonged. Nuclear vacuolation or vesiculation became common after long exposure or survival. The intermuscular spaces were usually wide, but contained no adventitious cells, except under the most severe conditions, when extravasated erythrocytes were found.

Fröhlich (1923) tested the effect of radioactive substances on the heart, of which the contractility, and hence the power to respond to stimulation, had been previously diminished. At first mesothorium was added to the nutritive fluid, but the impurity of the commercial product and the difficulty of causing precipitation of the barium contained in commercial

mesothorium led Fröhlich to abandon its use and to employ Ringer's solution containing radium emanation. The first series of experiments were carried out, in October and November, on the hearts of four *Ranae esculentae*, isolated according to the method of Straub and injured by being made to work in a cool chamber at a temperature between 8° and 10°C., for from three to twenty-four hours, without renewing the Ringer's solution and without replenishing the air or oxygen in the cannula. Under such conditions cardiac function was often maintained longer than forty-eight hours, but evidence of severe injury appeared much earlier and was characterized by loss of tone, dilatation, functional dissociation, weakening of the cardiac impulse, diminished amplitude of ventricular excursion, decrease in frequency, and arrhythmia, such as irregular systole. Dripping of Ringer's solution, containing from 15,000 to 30,000 Mache units of radium emanation, on the sinus and ventricles, or perfusion with such a solution, invariably caused an acceleration of cardiac contraction, which sometimes became regular and approximated the normal.

Another series of experiments was conducted on the isolated heart of rats. Five hearts were first subjected to the unfavorable influence of perfusion with unwarmed blood-Ringer mixture at a room temperature of 20°C. and at a pressure of 60 mm. of mercury. Subsequent perfusion with a similar mixture, containing from 1.8 to 2.7 million Mache units of radium emanation per hundred cubic centimeters, caused the heart to recover regular rhythmic activity, which previously had been partially or completely arrested. The heart of one rat was first perfused with Ringer's solution and grape sugar at 20°C., but with the addition of defibrinated blood. This was followed by arrhythmia and finally by complete diastolic relaxation. Perfusion with Ringer's solution containing grape sugar and about 2.2 million Mache units of radium emanation, but no blood, caused almost complete recovery of cardiac activity with regular rhythm. Fröhlich concluded that small doses of alpha rays from radium emanation in solution exert a favorable influence on cardiac activity, increase its ability to react to stimuli, and assumed that this was due to improved conduction. He admitted the important influence of potassium on the heart, but could not agree with Zwaardemaker, who contended that the action of potassium is necessarily indirect, and deduced that, while the effect of potassium is due to specific ions, the influence of radium emanation is "atomic" and differs in that it involves a destruction of energy. This deduction was based on the fact that the irradiative equivalent of two million Mache units in 100 c.c. of Ringer's solution would correspond to many kilograms of potassium in the same quantity of solution.

Coryllos, Edwards, and Bagg (1923), in investigating the feasibility of surgical dilatation of the mitral orifice to relieve functional embarrassment of the heart caused by mitral stenosis, attempted to produce, in dogs,[75] a progressive stenosis of this cardiac orifice. Doses of from 200 to 400 millicuries of radium emanation,[76] applied directly to the A-V valves and introduced in a special applicator through the appendix, gave promising results. Marked congestion and edema of the entire valve, including the base, and a patchy thickening at the border of the other leaflets resulted.

Viale (1923–1924), stimulated by the work of Zwaardemaker, sought to ascertain if uranium or thorium exerts on the living, isolated heart the same paralyzing, exciting, and antitoxic action as calcium; if the action of uranium on the heart, the pulsation of which has ceased for lack of potassium, is of an atomic or ionic order; and if this is derived from the uranium ion or from the radioactive elements of the metal. Without describing the technique employed, Viale stated that, in the first series of experiments, the heart of the frog was subjected to different experimental conditions by causing solutions of radioactive salts to act on the surface of the myocardium. On the heart perfused with the animal's own blood, in which potassium exerts an exciting effect, with slowing of rhythm and increased amplitude of contraction, neither uranium nor thorium had any such effect, but, contrary to the finding

[75] The number of animals was not stated.

[76] The filtration, time of exposure, and other important details were not mentioned.

of Zwaardemaker, a fall in the pulse rate was sometimes noted. On the heart of young frogs potassium almost always had a negative inotropic and chronotropic action; uranium, a positive inotropic and a negative chronotropic action; and thorium, a positive chronotropic action. Such difference in action was astonishing, in view of the fact that uranium and thorium emit the same radiations. On the heart stopped in diastole by NaCl the salts of potassium, uranium, or thorium did not induce the organ to resume its pulsation, while calcium chloride did. When cardiac contraction had been arrested by an excess of calcium salts, potassium chloride caused a revival of contraction; salts of uranium and thorium, even when allowed to act for a long time, remained ineffectual. When cardiac pulsation had been arrested in diastole by the first ligature of Stannius, salts of uranium, uranyl, and thorium never revived this function of the organ; mixing potassium chloride with salts of uranium or thorium did not neutralize the effect of potassium; hence this effect could hardly be due to antagonism between the *beta* rays of potassium and the *alpha* rays of uranium. Uranium and thorium almost never had any effect on the heart, the rhythmic contraction of which had been arrested by potassium after its pulsation had been revived by the second ligature of Stannius. Viale was unable to confirm Zwaardemaker's hypothesis.

To determine if the action of uranium on the heart was ionic or radioactive in character, Viale selected sodium uranate (UrO_4Na_2), in which the uranium functions not as a cation but as an anion group, on the assumption that, if the property of uranium should be due to its radioactivity, its biologic effects should be the same whether the uranium was an anion or a cation, providing the quality of salt in the perfusing liquid should be suitably equiradioactive. Experiments on frogs, in summer and winter, with Ringer's solution containing 0.003 gm. of sodium uranate per liter, showed that a transient increase in rhythm, frequency, and tone could be obtained by substituting an equiradioactive dose of sodium uranate for the potassium in the solution. Similar effects were noted with salts of uranium and uranyl, in which the metal acts as a cation. The so-called "paradoxical phenomenon" of Zwaardemaker did not appear as a characteristic effect of radioactivity, because the same phenomenon was observed after substituting potassium for the uranate, or vice versa; it could also be produced by withholding potassium from the heart. Viale thought this due to a modification in the colloids of the heart, because a similar phenomenon occurred whenever the composition of the perfusing solution was changed, such as substitution of a solution of sodium chloride for serum.

Zwaardemaker and Zeehuisen (1924) studied the effect of varying the dose of potassium and altering the temperature of the perfusing solutions. In twenty experiments on the heart of frogs[77] the Ringer's solution flowed through a system of glass tubes within a larger glass cylinder filled with water at a temperature of from 10° to 12°C.; the heart was outside the glass cylinder, near a Kronecker cannula, and the pressure within the organ was not more than 8 cm. of water. A second series of experiments was carried out on thirty hearts with a thermostat filled with water at constant temperature, in which the system of glass tubes, supplemented by a zinc vessel with openings above and below leading to the recording mechanism, was placed below the thermostat, which was attached to the apex of the heart by means of a thread (in the recording apparatus). The heart was attached to a Symes cannula, pulsated in the dark, and was shielded from air currents. Uniform heart action could generally be obtained by varying the quantity of potassium or by raising the temperature of the thermostat. So-called "group" action occurred when the temperature fell. The hydrogen ion concentration was maintained at a constant level of 7.4 by means of neutral red solution, and the perfusion rate was uniform, as determined quantitatively by registration. The cardiac effect of the non-radioactive elements, Ca and Na, and the radioactive element[78] and its substitutes, uranium and thorium, were tested, care being taken to keep the osmotic

[77] During the summer.
[78] Potassium.

tension of the Ringer's solution constant by replacing the electrolytes with equimolecular amounts of cane sugar; the sodium chloride was slightly decreased by adding electrolyte. The optimal limits of $CaCl_2$[79] lay between 1:10,000 and 1:4000. Less than 60 mg. or more than 275 mg. of water-free $CaCl_2$ per liter caused the frequency to diminish. This applied equally to the NaCl, which could vary between 7 and 4.5 without influencing the rate of pulsation. The effect of variation in potassium on cardiac frequency could best be observed by starting with a potassium-free solution and increasing it slowly or rapidly, according to the behavior of the organ. Each heart had a maximal frequency peculiar to itself. Different hearts showed optimal frequency with a small, medium, or large dose; one group, in which the maximal frequency was obtained with less than 0.100 gm. of KCl (between 0.050 and 0.080 gm.); a second group in which the maximal frequency was obtained with 0.100 gm. of KCl (toxic dose, between 0.250 and 0.300 gm.); and a third group, in which pulsation was arrested by NaCl or small doses of KCl (0.050 to 0.100 gm.), and regular pulsation was not resumed until the quantity of KCl was increased to from 0.200 to 0.350 gm. per liter of solution. After several hours, some hearts reacted differently to potassium and would then fall in a higher or lower group; the reaction of other hearts remained the same for five or six hours.

The influence of potassium on the heart of the lamprey was even more distinct, and the increase in frequency was proportional to the quantity of potassium. Of thirteen similar experiments with uranyl nitrate eight yielded typical curves. The frequency of a typical potassium heart was from 14 to 19; of a typical uranium heart, from 10 to 19. Some experiments with thorium also were tried, with essentially similar results, and the deduction was drawn that the action of the radioactive elements, potassium, uranium, and thorium, was quite different from that of calcium and sodium. With the latter the rate of cardiac pulsation was not altered, in spite of great variation in quantity of the element. With the former, on the contrary, the frequency changed with the quantity of element. Typical curves, obtained with potassium, showed maximum and minimum frequency with solutions containing between 0.025 and 0.500 gm. of salt per liter; in the case of uranyl, with solutions containing between 0.005 and 0.030 gm. of salt per liter; and in the case of thorium, with between 0.030 and 0.050 gm. of salt per liter.

Within the range of balance the frequency of pulsation was governed by (a) the temperature; (b) the quantity of potassium in the solution; (c) the previous condition of the heart; and (d) the rate of perfusion in so far as it influenced the amplitude of systole. In prolonged experiments various influences came into play, such as cardiac fatigue, the addition of lecithin and glucose and of impurities due to potassium or other cations. Such hearts, as well as organs in which any radioactive element might still be present, could not be used for fresh experiments. A transient increase in frequency of pulsation sometimes occurred on perfusion with potassium-free Ringer's solution soon after the heart had been removed from the body of the frog. This was also noted after the organ had been exposed for a long time to a solution containing a relatively large quantity of potassium. The relative effect of variation in temperature and of the strength of potassium and uranium on cardiac frequency was also investigated. Lowering the temperature of the heart in the thermostat 2°C. or less, by adding cold water to the space surrounding the air cylinder, decreased the rate of pulsation. When the original quantity of potassium or uranium corresponded to that of the zone of increasing frequency, but less than the maximal dose, an increase in the quantity of these radioactive elements also caused an increase in the rate of pulsation, so that the quantity of element corresponding to a difference of one degree in temperature could be determined. In five such experiments with potassium a decrease in temperature of 1°C. corresponded to a dose of approximately 0.060 gm. of KCl; the rate of pulsation was thus increased one beat per minute, on the average. In six experiments with uranium a drop in temperature of 1°C. corresponded to a dose of 0.0138 gm. of the element, and the cardiac rate was increased about two and one-half pulsations per minute.

[79] Water-free.

Zwaardemaker and Zeehuisen concluded that so-called "group" contractions, in a heart perfused with Ringer's solution, can be made regular by altering the quantity of radioactive substance in the solution; that each perfused heart has a specific rate of response to a given dose of radioactive element in the Ringer's solution; that, other things being equal, the optimal frequency is the same with alpha and beta rays; and that the frequency varies with the temperature and with the proportion of radioactive element in the solution.

ZWAARDEMAKER (1924) undertook to study the effect of radiant energy on the vagus control of the heart on *Petromyzon fluviatilis*, in which Carlson (1906) had discovered that the central nervous system may exert on the heart accelerating and probably also inhibitory influences. The initial trials were unsuccessful, but later Zwaardemaker was able to demonstrate the presence of accelerator and inhibitor nerves. The skeletal muscles of the animal were first paralyzed by injecting 0.004 gm. of curare into the peritoneum, after which the animal was left alone until all position reflexes had disappeared. The brain was then separated from the remainder of the nervous system by section behind both eyes. The brain and spinal cord were then exposed as far as the second branchial cleft. A straight glass cannula was placed in the right vena cava, and the animal, stretched on its belly, was perfused for a time with Ringer's solution containing 6.5 gm. of NaCl, 0.200 gm. of $NaHCO_3$, 0.200 gm. of $CaCl_2$, and 0.200 gm. of KCl. The excess of curare was thus eliminated little by little. The auricle was attached to a lever, under the animal, through an opening in the cartilaginous pericardium. Two slender platinum electrodes were then fixed in full view at the bottom of the fourth ventricle, at the site of the recording pen, where the vagus center is situated. In strongly curarized animals, a fairly long time often elapsed before any visible action occurred. At this moment the animal was completely quiet and it was certain that only the movements of the heart should register. The electrodes were connected to the secondary of a Dubois-Raymond sliding coil, equipped with a Neef hammer. The primary circuit contained an accumulator. The Pfeil signal, which was sometimes employed, could not be placed in shunt, but was arranged in the primary circuit. The distance of the coils was greater, therefore, than when the signal was interposed. This mode of excitation re-established cardiac synapsis under the influence of Ringer's solution sooner than that of the motor muscles, so that it was possible to observe the influence of excitation of the vagus center without any peripheral manifestation of the inevitable irritation of other nuclei and paths. Movements of the branchial pocket, which was also supplied by the vagus nerve, obviously could not be avoided, but, contrary to the findings of Carlson, this did not interfere. The first experiment showed that the vagus was excitable when perfused with uranium. Thus, during the long excitation of a heart perfused with 0.015 gm. of $UO(NO_3)_2$ per liter, the heart behaved exactly the same as during normal perfusion. In this animal the accelerating effect always preceded arrest of the vagus, which invariably occurred afterward. Since an isolated arrest of the vagus had been observed after previous acceleration, the arrest could not be defined as an "after effect" of acceleration. When the excitation was maintained, the result was an "escape" of the vagus, and the heart continued to beat regularly. This succession of facts confirmed the observations of Lely. But to prove absolutely that radiant energy is necessary to excite the vagus, it was necessary to show that the excitability disappears on inactive perfusion, but is re-established by alpha rays, as was shown by Lely. Under such circumstances, however, the curarization produced a disagreeable complication. Since the curare was constantly eliminated, the indirect sensitiveness of the striated muscles to electrical excitation also became continuously greater. This made it impossible to use curarized animals to study variations in excitability. After having found empirically the exact technique, curare was discarded, and if necessary the interfering movements of the animal were allowed. As Schiff had found with the frog, it was noted that, with *Petromyzon* also, the excitability of the vagus disappeared after irrigation with potassium. The pulsations first underwent a strong negative

Journal Page 318

chronotropic influence, but the same excitation had no effect after perfusion with a liquid free from potassium. The inotropic action lasted longer than the chronotropic.

When, after a diminution in excitability, the heart was perfused with Ringer's solution containing uranium, the excitability of the vagus reappeared in a large number of cases, as indicated by Lely; but at the same time, after each excitation the inotropic restoration was delayed for a long time and finally did not appear at all. If at this stage potassium was added, the cardiac forces were restored. Everything occurred as if, on excitation of the vagus, a substance regenerating well in the presence of potassium, but not of uranium, and which was of capital importance to cardiac energy, had been withdrawn from the heart. This substance was represented as a compound of potassium, which is eliminated, an hypothesis related to the ideas of Howell.

Summed up the results were as follows: (1) The cardiac branches of the vagus could be excited by perfusion with Ringer's solution with potassium and with a solution free from potassium, but containing uranium. (2) In certain cases the vagus was not excited by perfusion with Ringer's solution containing potassium, but was excited by a solution containing uranium. (3) In *Petromyzon fluviatilis*, excitation of the nucleus of the vagus was generally followed first by acceleration, then by slowing or arrest. In some cases acceleration did not occur, but only an isolated, negative chronotropic effect was noted. In other cases only acceleration of rhythm was observed. (4) A cardiac branch of the vagus was excited by perfusion with Ringer's solution containing potassium, but lost its excitability when the heart was perfused with a liquid free from potassium. The vagus effect was re-established after addition of an equiradioactive quantity of uranium. (5) Repeated excitation of the vagus in the uranium state diminished cardiac energy. These facts were held not to contradict the views of Howell, according to which, when the vagus is excited, potassium is liberated in such quantity that a local, transient intoxication due to potassium occurs.

KAWASHIMA (1924) tested the action of thorium emanation and its products of disintegration, thorium A, B, C, C_1, and D (alpha, beta, and gamma rays) on the isolated heart of sixteen frogs. Each animal was killed by destruction of the nervous system, and the heart was freely exposed, care being taken to prevent any direct or indirect contact between the organ and the skin. After opening the pericardium, a thread was passed under the left aorta, the vessel was opened, and a glass cannula filled with Ringer's solution was placed first in the aorta, then under the bulbus arteriosus, and finally pushed until the tip lay within the ventricle. The thread was tied, and the excised heart hanging on the cannula was placed in a Straub chamber. The movements of the ventricle were transmitted, by means of a thread fixed to the apex of the heart with a pair of fine forceps, to a light lever, the excursions of which were recorded on the smoked drum of a kymograph. Oxygen containing thorium emanation was made to flow continuously into the Straub chamber. This was accomplished by placing a solution of radiothorium in a gas-washing bottle, in which the quantity of radiothorium in solution was in equilibrium with its first product of disintegration, thorium X, which formed thorium emanation continuously. The constant stream of oxygen removed the emanation from the solution, carried it into the Straub chamber, and maintained a steady concentration of radioactive substance. The radioactivity was sufficient to kill a rabbit within twenty-four hours.[80] In order to provide control conditions, Kawashima arranged a system of three channels, through which the heart in the Straub chamber could be alternately surrounded by an atmosphere of pure oxygen for ten minutes, one containing alpha, beta, and gamma rays for thirty minutes, and again by pure oxygen. Kawashima found it impossible to influence the heart of frogs in the Straub chamber, even by strong irradiation.

ZWAARDEMAKER (1925), on the assumption that the small quantity of potassium present in the heart of the frog is radioactive, and that the irregular pulsations occurring when the

[80] The dose was not otherwise specified.

heart is perfused with normal Ringer's solution were due to the influence of the radioactive particles acting chiefly on the sensitive auriculo-ventricular node, attempted to find an explanation for the transient paradoxical disturbance in cardiac function at the moment when the Ringer's solution containing only a small quantity of potassium was changed to a solution containing more radioactive substance; for the long-continued arrest of function which followed perfusion with equal parts of the foregoing solutions, and for the immediate change resulting from the addition or subtraction of potassium or other radioactive elements. It was assumed further that such transient arrest of cardiac pulsation must have a physical, or radioactive, and not a chemical basis. This apparent paradox was constant in winter, but often did not occur during the summer. To test this on a larger scale, the heart of frogs (summer) as perfused alternately with Ringer's solution containing 0.2 per cent of potassium and with solution containing radium emanation.[81] The experimental conditions were otherwise the same. In sixty-three transitions from potassium to emanation solutions, the paradox appeared eighteen times; in fifty-nine transitions from emanation to potassium solutions the paradoxical disturbance occurred twenty-two times. Thus, a transient cessation of pulsation at the moment of changing from one solution[82] to the other was noted in approximately one-third of the tests. Addition of adrenalin, in a concentration of one per million, caused the reversible paradoxical reaction to disappear for a short time, after which it reappeared. An attempt was made to duplicate this effect with cholin, but without success. It was therefore deduced that the initial rhythmic contraction of the heart was due to the presence in the cardiac tissue of an adrenalin-like hormone which maintained the cardiac rhythm for some time after the composition of the perfusing solution had been modified (changed from one solution to the other). Zwaardemaker thought this latent period was due to the approximately equal amount of radioactivity in the two solutions allowing the hormone to maintain contraction, but that later the hormone was washed out and this caused a temporary torpor of the heart, which continued until sufficient radioactivity had accumulated.

Goodrich and Scott (1925) studied the effect of the beta and gamma rays emitted by a glazed plaque measuring 20 by 20 millimeters and containing 15.1 milligrams of radium barium sulphate, representing 10.3 milligrams of radium element, on the heart of eight-day old chick embryos. These were removed in a warm chamber under aseptic conditions, cut into small pieces, and placed in Ringer's solution in glass depression slides. The radium plaque was placed over the slides without the intervention of a cover slip or filter of any kind, so that the tissue received all the gamma and all but the softest beta rays. The distance between the plaque and the tissue varied between actual contact and 2 mm. (average, slightly more than 1 mm.). The slide was then placed in a moist chamber in an incubator, and a similar slide of control tissue was kept under identical conditions, but protected with a sheet of lead.[83] At definite intervals pieces of tissue were removed from each slide and planted in hanging drops of chicken plasma diluted with an equal amount of distilled water. At the end of twenty-four hours, the cultures were inspected to determine the amount and character of growth (wandering ameboid cells), and several slides of each group were fixed in osmic acid vapor and stained. This was repeated after forty-eight and seventy-two hours, until it was established that no further change occurred after forty-eight hours. The cultures were not carried beyond seventy-two hours. The character of growth in the control and treated cultures was always the same, and in almost every group all the control and irradiated cultures showed an equal amount of active wandering. No effect of the radium on the rhythmic contraction of muscle cells, noted in many cultures, was observed. When the stained cultures

[81] The emanation was derived from uranium salts (uranyl nitrate).

[82] The potassium Ringer's solution contained from 0.050 to 0.150 gm. of KCl per liter and the emanation solution from 0.005 to 0.030 gm. of uranyl nitrate per liter, besides 6.5 mg. of NaCl, 0.200 gm. of water-free $CaCl_2$ and 0.200 gm. of $NaHCO_3$.

[83] The thickness of the lead was not stated.

were examined, however, the radium was found to have had a definite effect on the number of cells in mitosis; this was the prominent feature. Exposure to radium for four hours had little or no effect, but mitosis was inhibited by exposure for five or six hours. Thus the minimum lethal dose appeared to be between four and five hours. No difference of effect from the slight variation in distance was found. The effect of a circular applicator was approximately equal to that of a square of the same area. Comparison of the foregoing results with those obtained by Wood and Prime, on the basis of formulae prepared by Harris and by Quimby, indicated "a considerable effect of the soft beta rays," which, in the experiments of Wood and Prime, had been absorbed by the cover glass.

Zwaardemaker (1925), without describing his experiments, and assuming that, as far as the influence on cardiac function is concerned, potassium may be replaced by other radioactive elements, the cardiac activity induced by cesium was due to impurities or to potassium stored in the tissues or in circulation, undertook to study the problem further. Ringer's solution containing radium emanation in lower concentration than that present in the organs was employed. The preparations were sufficiently radioactive to sterilize a culture of luminous bacilli in a few hours, and some of the cells of the heart were also injured. The heart resumed pulsation only temporarily. The alpha rays emitted by polonium had less effect, but, however great was the effect around the source of the alpha rays, the sensitive tissue of the auriculo-ventricular node was less influenced. Once the rhythmic pulsations were initiated by irradiation, however, they often continued regularly for many hours. Zwaardemaker advanced the hypothesis that the automatic function of the heart is maintained by one explosion per second of an atom of potassium stored in the tissues or in circulation (not the potassium in the perfusing fluid). If an excess of potassium is present, the effect is injurious and the pulsations cease or become less rapid. But he admitted that this fails to explain why cardiac function was not revived when the radioactive content of the solution was less than 0.001 gm. of radium element and why this was ineffective at a distance greater than 2 cm.

Borman (1927) sought to ascertain the effect of radium emanation on the sino-auricular node and adjacent cardiac tissue of dogs, hoping thereby to obtain information concerning the intimate structure of the node and to determine whether or not the node is more primitive in structure than the surrounding cardiac muscle. Under aseptic precautions and intermittent, intratracheal, air-ether insufflation with an Erlanger respiratory tank, 4 cm. of the right third and fourth ribs of fourteen dogs were resected from the region of the costochondral articulation, the pleura incised, and the exposed pericardial sac was opened and its margins temporarily sutured to the edges of the wound. To expose the junction of the superior vena cava and right auricle, the heart was rotated on its longitudinal axis by a suture through the fat in the auriculo-ventricular groove passing out through the chest anteriorly. A small glass tube containing from 0.6 to 5.0 millicuries of radium emanation and enclosed within a second larger glass tube 1 mm. in diameter and 10 mm. in length was inserted, with blunt forceps, beneath the epicardium over the sino-auricular node and left in position. The animals were allowed to recover, and a necropsy was performed from eight hours to eight months after insertion of the radon. The fresh sino-auricular tissue was fixed in 10 per cent formalin, mounted in paraffin, and serial sections 10 micra thick were cut transversely to the long axis of the linea terminalis. Some were stained with hematoxylin and eosin, and others with Van Gieson's stain, hematoxylin being used to bring out the nuclear structures.

The tube of radon, in one animal which had received a dose of 666 millicurie-hours and which died ten days after the tube of radon had been introduced, was surrounded by a grayish colored area extending 2 cm. from the tube. This grayish area of necrosis and degeneration was itself surrounded by a hemorrhagic zone. Other changes included marked hyperemia, moderate erythrocytic infiltration probably from rupture of capillaries, marked

vascular and perivascular degeneration, numerous punctate hemorrhages, and proliferation of connective tissue. The walls of the nutrient vessel of the sino-auricular node were necrotic, but the internal and external elastic membranes were remarkably preserved. Examination of a second dog, killed with ether 180 days after the introduction of a glass tube containing 2 millicuries of radium emanation, showed a zone of degeneration, necrosis, and fibrosis extending 2 cm. from the position of the tube. Nodal tissue could not be identified, and the degeneration, which involved the entire crista terminalis, consisted of extensive hemorrhage, fatty degeneration, necrosis, advanced fibrosis with hyalinization and calcification, and occlusion of the central nutrient vessel of the node. Corresponding abnormalities were found in the other animals. Borman concluded that the sino-auricular node is more sensitive to radiation and, therefore, more primitive than the surrounding cardiac tissue; that the effect of small doses or the early effect of large doses is engorgement followed by rupture of the small blood vessels, with hemorrhage into the surrounding tissue; that the effects of radiation on the sino-auricular node and neighboring tissue are disturbances in circulation, fatty degeneration of cells, disintegration of nuclei, necrosis, proliferation of connective tissue, and calcification; and that these pathological changes suggest a primary action of radon on the cells and not an action secondary to circulatory disturbances.

Zwaardemaker and Zeehuisen (1927) investigated the frequency of contraction of the heart which, having ceased to pulsate as the result of perfusion with Ringer's solution devoid of potassium, was caused to pulsate again by exposure to varying doses of radiation. After having determined the frequency of contraction of the heart of the frog when perfused with Ringer's solution containing 0.100 gm. of potassium chloride per liter, the time required for the heart to stop beating when irrigated with Ringer's solution without potassium was ascertained. Finally, at different times, radium was placed in the immediate vicinity of the heart. Three radium preparations were in the form of flat plaques and contained 1.6, 1.8, and 1.9 milligrams of radium element, respectively. One preparation consisted of a glass capsule containing 3.3 milligrams of radium element, and another preparation consisted of a mica capsule covered with enamel and containing 3.4 milligrams of radium element. Exposure of the heart to radium, after the rhythmic contraction had been stopped by perfusion with potassium-free Ringer's solution, revived the pulsations, the frequency of which increased with the dose, from about eight contractions per minute with 3.4 mg. of radium to about thirteen contractions per minute with 8.6 mg. of radium.

In additional experiments, in which the effect of radium was superimposed on that of potassium, the rate of contraction was increased up to a maximum, but if the dose of radium was more than sufficient to attain this maximum, the increase in the rate of pulsation was not so great. This was tested on four series, with five frog hearts in each series. The hearts of the first and third series were perfused with Ringer's solution containing from 0.050 to 0.150 gm. of KCl without radium; those of the second series with the same solution containing 3.3 mg. of radium; and those of the fourth series with the same solution containing 6.7 mg. of radium. The variation in the quantity of potassium in the solution made it difficult to evaluate precisely the influence of radium on the rate of contraction, but an impression of interaction of the beta activity in the radium and in the solution was obtained from the tabulated results. Zwaardemaker and Zeehuisen concluded that cardiac pulsation, arrested by withdrawing potassium from the perfusing solution (Kronecker method), could be revived by exposing the organ to about 3.3 mg. of radium element; that small doses caused a slow increase in the rate of contraction, while the increase following large doses was not proportional; and that a certain interaction of potassium and radium was apparent.

Borman (1927), at the suggestion of J. E. Sweet, successfully used radium emanation to destroy the sino-auricular node of the heart in fourteen dogs. The emanation was in glass tubes about one centimeter in length, and the tubes were introduced "immediately beneath

the epicardium over the site of the sino-auricular node."[84] Borman observed that the node appeared more sensitive to radium emanation than the surrounding tissue and deduced that the node is embryologically more primitive. The elastic coats of the arteries displayed great resistance to such radiation. The pathologic changes noted were fatty degeneration, karyorrhexis, necrosis, and scar formation. The effects on the nodal cells and nuclei appeared primary as well as secondary to circulatory disturbances. The destruction of the node, which required thirty-three days, could not always be detected in the electrocardiogram. After destruction, the rhythm sometimes simulated the normal sinus rhythm.

ZWAARDEMAKER (1927) assumed that natural automatin, a beta-automatin, is derived from a mother substance present in heart muscle and, after activation, passes into the circulation and is the immediate cause of the automatic action of the heart. When an isolated heart is perfused with Ringer's solution in such a manner that the perfusing solution may run off, the automatin does not reach the circulation but, by diffusion, reaches the atrio-ventricular node of the Symes (eel) or Kronecker (frog) heart. If, instead of ordinary Ringer's solution, a calcium-free solution is used and the automatin thus completely washed out, the heart ceases to beat and some other source of radiation[85] is required to cause it to beat again. Provided the resting heart is not perfused too long, artificial irradiation activates the mother substance in the muscle. The activated automatinogen diffuses slowly to the atrio-ventricular node, and, if the quantity of the substance is sufficient, the ventricle begins to beat.

If the perfusing solution is made to pass through the heart again and again, and if the circuit requires from ten to twenty minutes, the supply of automatin tends to accumulate; this depends on the duration of perfusion and the quantity of circulating fluid. The substance may reach the nodal tissue by diffusion or through circulatory channels. The fluid may be withdrawn and used on another heart or another circulation; after a brief latent period, the second heart will also begin to beat. Such a radioactive solution may be diluted with calcium-free Ringer's solution two or three times; when diluted four times, it ceases to stimulate the second heart. Zwaardemaker thought such action cannot depend on the concentration of calcium ions because, after passing through the heart, the calcium concentration of the circulating fluids is never greater than two, and after passing through two hearts, never greater than three.

Automatin almost free from calcium can be obtained by absorbing the calcium in talcum venetium (magnesium silicate) and extracting it in 96 per cent alcohol. After the alcohol has evaporated, the remaining substance is insoluble in ether and may thus be separated from lipoids; it is thermostabile, easily filtered, and may be kept for a few days. Mother substance may also be obtained from an unirradiated heart at rest; it has similar properties, but does not keep so well, and seldom produces a stimulative effect. Automatinogen may also be transformed into automatin by exposing a thin layer of a watery solution of automatinogen all night to three Email radioactive applicators (total, 5.3 mg. of radium element). The latent period is always short.

Two hearts were suspended in such a way that the upper, irradiated heart acted as donor, and the lower, unirradiated heart as receptor, of the automatin, with both hearts in one and the same circulation. Both hearts were arranged so that they recorded on the same smoked cylinder. The circulation was not started until both hearts were at rest. The heart which first came to rest was exposed either to the three Email radium units ($1.6+1.8+1.9=5.3$ mg. radium element) or to the three polonium precipitation flasks 1 cm. square. Such an experiment was repeated six times, and, without exception, the two hearts began to beat. After exposure to radium, the irradiated heart started to beat after an average latent period of thirty-two minutes, while after exposure to weak polonium radiation, the latent period varied

[84] No further details were given.

[85] Email radium carrier or polonium precipitate on copper strips surrounding the heart on three sides.

from sixteen minutes to six hours. The unirradiated heart began to beat about two minutes later.

From these experiments it was deduced that from the first heart there is added to the solution a substance (automatin) which causes the second heart to pulsate, and that there is little difference in the latent period and sequence of systoles between the two hearts.

Zwaardemaker stated that when one heart is exposed to radium and the other to polonium, according to the law of physiologic antagonism one should expect that neither of the two hearts will become active. This expectation was not fulfilled, because the influence on the two hearts of automatins of different kinds differed in intensity. One or another kind of automatin gained the upper hand and induced definite pulsations, but these did not last long. When the two hearts were exposed to mixed radioactive solutions of radium and of polonium, there followed a peculiar piling up of contractions. The experiment was characterized by a short latent period, a decrease in frequency to complete rest, and finally an increase in frequency to regular pulsation. Zwaardemaker felt compelled to attribute such results to an antagonism between alpha and beta automatin.

Analysis of Experimental Data

Roentgen Rays. The report of Sabrazès and Rivière (1897) that the heart of a frog was not influenced in its function, even by exposure to roentgen rays for one hour, is interesting from an historical point of view, but their failure to supply essential data concerning the dose of radiation and the conditions of exposure robs their report of any value.

The experiments of Allen (1903) indicate that irradiation of the freshly isolated and actively beating heart of cold-blooded animals has little effect on the function of the organ, but that in time cardiac pulsation diminishes, or ceases altogether. Unfortunately, the lack of parallel control experiments makes it impossible to know if the inhibition of function noted by Allen was a direct effect of irradiation, or if other factors, such as alterations in the temperature and moisture of the heart from the heat emitted by the tube, played a part in diminishing the rate and amplitude of contraction. The results obtained by Allen were not confirmed by Haberlandt and Sandera (1927), who found that irradiation of tissue excised from the sino-auricular portion of the heart, or from the base of the ventricle (heart of frog), caused an early, transient inhibition of contraction, followed by acceleration of cardiac pulsation, and tests with atropin apparently demonstrated that the initial inhibition was not due to action of the rays on the vagus. The deduction that acceleration of the heart beat indicated a favorable influence of radiation on the formation of cardiac hormone is speculatively interesting, but hardly rests on tangible evidence. On the contrary, the conclusion of Haberlandt and Sandera that the radiosensitiveness of the heart is slight has been repeatedly confirmed, as will be shown presently. The studies, by H. Zwaardemaker and Feenstra (1928), of the effect of unspecified, but probably very small, doses of soft roentgen rays (long wave-length) led them to deduce that irradiation activates automatinogen in the heart, whose pulsation has been stopped by perfusion with potassium-free Ringer's solution, to automatin which causes pulsation to return. Unfortunately, in many of these experiments positive results were obtained in only 30 per cent of the tests, and the authors admitted their inability to exclude the effect of heat. As will be seen later in connection with their experiments with radioactive substances, the ground for their deductions does not appear firm.

The well-controlled investigations of Heim (1928) clearly indicate that irradiation of chick embryos *in ovo* retards the growth of the organism, causes various deformities, and often leads to death. Such influence on growth has been definitely established by many other experiments. But when Heim attempted to determine the influence of roentgen rays on *in vitro* cultures of the heart of chick embryos irradiated while still in the egg, he found that the explants first grew as well as the controls and that a tendency to degeneration and increase in mitotic division subsequently became apparent, but that these effects were so inconstant that conclusions could not be drawn. Even if the changes described had occurred uniformly, this need not have meant a direct and primary effect of radiation on the cardiac tissue of the embryo. Indeed, it is much more probable that the influence on the cultures was indirect and secondary to the retarding effect on growth of the organism as a whole. This probability is considerably strengthened by the evidence furnished by Roffo (1924), who found that the growth of tissue cultures from the heart of chick embryos irradiated *in vitro* immediately after the tissue had been placed in plasma, and again twelve hours after culture, continued unimpeded, regardless of the duration of exposure to the rays. Attention should here be drawn to a circumstance mentioned by Roffo himself, which may possibly account for the failure of irradiation to influence his cultures. Roffo stated that a change in the medium in which the heart muscle cells grew may have altered their power to react. He also admitted the possibility that tissues isolated from the organism may not react in the same way, but these factors are apparently excluded by the fact that, in his experiments, the vitality of the tissues actually increased, and yet the cardiac tissue resisted irradiation.

In connection with the experiments of Heim and of Roffo, the investigations of Krontowski (1925) and of Schubert (1927) are decidedly interesting. Krontowski found that irradiation of eggs containing four-day-old embryos caused them to die, but, regardless of whether the embryos were dying or actually dead at the time the cultures were made, and in spite of the fact that the heart was sometimes speckled with petechial hemorrhages, the cultures grew well, and the explanted cardiac tissue contracted rhythmically for the duration of the experiment. This tends to prove that the lethal effect of the rays was not primarily on the heart, and that the hemorrhages noted in the organ were probably secondary to changes in other, more sensitive, structures. Schubert not only confirmed the work of Krontowski, but, by extending the scope of his studies, was apparently able to demonstrate that the time between irradiation and culture determines the success or failure of the cultures. Evidence of retardation or cessation of growth also was obtained, and this effect on embryos irradiated *in ovo*, as well as *in vivo*, was likewise shown to depend on the time factor. Schubert had reason to conclude, therefore, that such changes as he had observed were not specific effects of roentgen irradiation on the cardiac tissue, but probably were due to the circulation of products of cellular decomposition from other organs or tissues.

The studies of Karczag, von Farkas, and Györgyi (1927) indicate that the colloido-chemical or physico-chemical disturbances which may be induced in the heart by irradiation under ordinary conditions fall within physiologic limits and are disposed of in the ordinary course of metabolism.

The results reported by Swann (1924) are confusing, and their interpretation,

at best, uncertain. There are reasons for believing that the fall in blood pressure was not a direct effect of irradiation. As will be seen later, exposure to roentgen rays does not appear to influence blood pressure directly, but an indirect influence may result from irradiation sufficient to induce pronounced radiation sickness and depression of general metabolism. Nor is it clear, in the absence of detailed post-mortem records and of careful histo-pathologic examination of the various organs, why the animals should have died from cardiac failure. The same reasons make it difficult to understand why the isolated heart of frogs and rabbits should have behaved so differently. Such lack of uniformity in the results makes us pause to consider if this might not have been due to something besides irradiation. The attribution of death in systole to plugging of the coronary vessels or to muscular contraction is purely speculative and rests on insufficient evidence. This is especially true if we take into account Swann's statement that the flow through the coronary vessels actually increased. Moreover, Swann did not explain the contraction of the cardiac muscle and the concomitant constriction of the bronchial muscles, tonic contraction of the uterus, and increase in tone of the intestine. His observation that the sympathetic nerves became more sensitive after short, and less sensitive after prolonged, exposures to roentgen rays also may have played a part, but such action on the sympathetic nerves need not have been a direct effect of irradiation. The results obtained by Swann would be decidedly puzzling had not Stephens and Florey (1927) furnished evidence that some of Swann's discrepancies were due, not to a direct or indirect action of roentgen rays, but to the influence of high-tension electrical discharges. This at once explains the contraction of the heart, the fall in blood pressure, the constriction of the bronchial muscles, and the tonic contraction of the uterus. When Stephens and Florey excluded the possible influence of electrical discharges by shielding the animal with a suitable electrical screen, effects such as those described by Swann could not be obtained. But even when the animals were irradiated without the electrical screen, only a slight, continuous fall in blood pressure was noted. Moreover, their results, so far as direct irradiation of the heart is concerned, contradict those of Swann and show that prolonged exposure to roentgen rays does not have any immediate perceptible effect on its function.

The attempt of Hallheimer and Schinz (1925) to determine the influence of roentgen rays on the oxidases in cardiac muscle also was fruitless; they were unable to perceive any uniform difference in the behavior of irradiated and unirradiated sections of the heart.

The experiments of Warren and Whipple (1922), Davis (1924), Gordon, Strong, and Emery (1924), Tsuzuki (1926), Hartman, Bolliger, Doub, and Smith (1927), Warthin and Pohle (1927), Domagk (1928), and Warthin and Pohle (1929), must be considered as a separate group, because they all relate to the effect of roentgen rays on the adult heart. The diversity of results may appear confusing until the details of the experiments are closely scrutinized. Warren and Whipple, and Gordon, Strong, and Emery were unable to find distinct functional or organic abnormality in the heart of dogs or rabbits after exposure of a small portion (precordium) or all of the thorax. Gordon, Strong, and Emery, it is true, noted small areas of fatty degeneration or necrosis in the heart muscle, which, they thought, resembled the cardiac changes described by MacCallum as incidental to various infections, intoxications, and nutritional disturbances. Such alterations may have been indirectly

due to irradiation, but there is no good reason to think that they represented a direct effect of the rays on the heart. This view is strengthened by the investigations of Tsuzuki (1926), Warthin and Pohle (1927), and Domagk (1928). Tsuzuki exposed the entire body of many rabbits to from 10 to 160 per cent of the human erythema dose, and found extensive pathologic changes in the lymphoid structures, genital glands, lungs, kidneys, liver and bone marrow, but in the heart only fatty degeneration was noted. Warthin and Pohle exposed the cardiac region of rats and rabbits to from 100 to 1000 per cent of the human erythema dose. The only abnormalities observed by them also were fatty degeneration and necrosis, and in a few animals these alterations were marked and might readily have been regarded as effects of irradiation had not the heart of unirradiated, control animals exhibited the same degenerative and necrotic changes. Warthin and Pohle were undoubtedly justified in considering the Zenker necrosis as an agonal condition, possibly increased by fixation of the beating heart in formaldehyde solution, and fatty degeneration as the expression of a nutritional state rather than as a primary or direct effect of irradiation. As they concluded, there was no evidence that a single exposure of the heart even to an enormous dose of roentgen rays causes definite injury to the heart muscle of adult rats and rabbits. The only possible deduction seems to be that the fatty degeneration and necrosis noted under the conditions described had no direct or even indirect relation to irradiation; in other words, these changes were not specific effects of roentgen rays, but were due to factors commonly present in unirradiated animals. Domagk also found fatty degeneration and necrosis, and, after a time, interstitial proliferation of fibroblasts.

The studies of Davis (1924) bore primarily on the action of excessive doses of roentgen rays on the lungs and pleura, and will be discussed in relation to these structures. They are mentioned here only because, in one rabbit, the pericardium contained an abnormal quantity of fluid and presented fibrinous adhesions, and in all but two of the dogs, thickening of the anterior wall of the right auricle was represented microscopically by areas of necrosis, hemorrhagic extravasation, and hyalinization of some of the cardiac muscle fibers. Considering the acute and marked inflammatory reaction of the lungs and pleura to excessive roentgen irradiation, noted by Davis in all his animals, the serofibrinous pericarditis observed in only one of several irradiated rabbits does not appear to have been a direct or specific effect of the rays on the heart, but was probably a reaction of the pericardium to the inflammatory process in the adjacent lung and pleura. In the case of the dogs, the thickening of the anterior wall of the right auricle, the areas of necrosis, hemorrhage, and hyaline degeneration of some of the cardiac fibers might also be regarded as indirect results of the pathologic changes induced in the lungs and pleura by excessive irradiation, were it not that these abnormalities were apparently confined to a portion of the organ. This circumstance points to a direct, rather than to an indirect, influence, unless it should be accounted for by proximity of this part of the heart to the overlapping portion of the right lung, which bore the brunt of irradiation and reacted accordingly. A direct, specific action of the rays, to account for the cardiac changes described, would be hard to accept, however, unless analogous changes had been observed in both rabbits and dogs. The absence of cardiac abnormalities in the majority of the rabbits leads to the deduction that a difference in anatomic relation-

ship between the lungs and heart in the rabbit and dog may perhaps explain the discrepancy.

In a later series of experiments, Warthin and Pohle (1929) exposed the precordial region of rats and rabbits to an initial dose of 600 r and to two subsequent doses of 300 r at intervals of one month. A dose of 600 r represents the so-called tolerance dose for human skin. This fact is not significant in itself. What may be significant is the great difference in thickness between the human body and that of a rat or even of a rabbit. If, as is well known, a considerable percentage of the quantity of such rays striking the surface of the field of irradiation penetrates the human body to a depth of 10 centimeters, it must be obvious that a much larger percentage of the surface dose must pass completely through the body of a rat and only a slightly lower percentage through the body of a rabbit. The conditions cannot by any stretch of the imagination be regarded as identical. In the case of the rat and rabbit, such a dose must be several times greater and its effects should be several times more pronounced. One factor, however, may partly compensate for the comparative difference in thickness of body, i.e. in the mass of tissue irradiated, between the rat or rabbit and the human being; this is the surface area exposed. But the conditions of the experiment specify that the skin tolerance dose in the human being, with the same technical factors, was 300 r; this would imply that the surface area was the same. If so, the smaller body of the rats and rabbits received, through the precordial area exposed to the rays, a much greater actual dose.

Warthin and Pohle found, in the myocardium of their animals, more pronounced hyaline degeneration, necrosis, and fatty degeneration than in their previous experiments (1927), and varying degrees of inflammatory reaction and early interstitial proliferation. They thought these abnormalities were comparable with those observed in the human heart following diphtheritic toxemia. Moreover, a correct interpretation of these pathologic changes was made difficult by the common presence of catarrhal or purulent bronchitis and bronchopneumonia, affecting especially the main bronchi and the portions of the lungs occupying the anterior mediastinum, local or general mediastinitis, pleuritis and pericarditis. Another important point is that, among both the irradiated and control animals, bronchial and pulmonary infection was almost universal. It was assumed that the inflammatory disturbances in the bronchi, lungs, pleura and pericardium began in the irradiated animals and were transmitted to the control animals through infected exudates. Irradiation was thought to injure the bronchi and lower the resistance of the animals; infective bronchitis and bronchopneumonia developed and increased the myocardial damage which they regarded as a primary and direct effect of irradiation. "Unfortunately, similar pulmonary lesions were found in the majority of the controls, and in some of these the same type of myocardial lesions of a less severe degree."

The more these experimental findings are scrutinized the more likely it appears that irradiation affected first the pleura and lungs, especially the portions occupying the anterior mediastinum, which received the largest dose of rays; that the resulting inflammatory reaction extended, through secondary infection, to other portions of the lung, and that the myocardial abnormalities were only indirectly related to irradiation. Important also to remember are the destruction of lymphoid cells and hyperplasia of reticulo-endothelial cells which were found in the thymus gland and mediastinal lymph nodes, together with fat necrosis, chromatolysis and lipoidosis

of ganglions, and edema of nerve trunks in the mediastinum of the irradiated animals only. There is little doubt that the pleuro-pneumonitis was a primary and direct result of irradiation, but it does not necessarily follow that the mediastinitis, pericarditis, and the myocardial changes also, were a direct effect of exposure to the rays; indeed, the weight of evidence indicates that the degenerative abnormalities in the mediastinum, pericardium, and myocardium were not directly caused by irradiation, but were secondary to alterations in the pleura, lungs, thymus gland, lymph nodes and other more sensitive tissues.

As has been previously mentioned, it is a fact well known to pathologists that varying degrees of fatty and hyaline degeneration of the myocardium are almost constant effects of nutritional and toxic disturbances; they are most commonly seen after infectious diseases. It is even probable that some of the cardiac complications of such infections are a measure of the fatty or hyaline degeneration present and that recovery is partly proportional to the disappearance of such changes. Any radiation injury to, and reactive inflammation of, the respiratory organs, especially when complicated by secondary infection, may therefore be logically expected to throw upon the heart, not only the mechanical burden of maintaining adequate aeration of the blood but also a more or less important toxic factor consisting partly of the products of pulmonary cellular disintegration and of those elaborated by bacterial action. Warthin and Pohle were undoubtedly right in considering infection of many of the control animals as due to bacterial transmission; one point in favor of this view is that the pulmonary and myocardial changes in the unirradiated rats and rabbits were not so marked or extensive; this probably means that the pulmonary infection and the resulting myocardial changes occurred later. But this also strengthens the view that the abnormalities found in the myocardium of the irradiated animals were indirect rather than direct results of exposure to the rays. The lungs are indubitably more radiosensitive than the heart; ample confirmatory evidence will be found in another section. Therefore, the conclusion that the myocardial alterations were due in large measure to irradiation does not appear sound. Warthin and Pohle seem to have been unduly influenced by the deductions of Hartman, Bolliger, Doub and Smith into confirming the possibility of injury to the myocardium by roentgen rays. The possibility cannot be doubted, but direct injury to the heart would seem to require a quantity of rays far in excess of the quantity ordinarily used in the treatment of human beings. Warthin and Pohle pertinently admitted that "as far as our own clinical experience is concerned, no roentgen-ray injury of the heart was observed at autopsy in patients who had been treated over the precordium." Moreover, their experiments do not warrant the inference that the heart is relatively sensitive to radiation. On the contrary, all evidence indicates that the heart is comparatively insensitive.

The evidence furnished by the foregoing experiments indicates that the heart can tolerate strong doses of roentgen rays, and that the specific radiosensitiveness of the organ is much less than that of the pleura and lungs. This is not intended to imply, however, that the heart is completely insensitive to radiation, regardless of the dose. When the investigations of Hartman, Bolliger, Doub, and Smith (1927) are considered, the first impression is that, at last, we have an example of the specific influence of roentgen rays on the heart. On analyzing the experimental conditions and the results, however, a measure of doubt is unescapable. With roentgen rays

generated under the conditions stated, the human erythema dose required an exposure of fifteen minutes (450 milliampere-minutes). A portion of the anterior thoracic wall of the dogs was actually exposed to from 2,250 to 8,400 milliampere-minutes, and of the sheep, to from 3,600 to 8,400 milliampere-minutes, or from five to over eighteen times the human erythema dose. It would be almost a miracle if the heart, or any other organ, could tolerate such irradiation. Under the circumstances, it is not surprising that Hartman, Bolliger, Doub, and Smith should have found, in the field of irradiation, passive hyperemia and edema of the thoracic tissues, passive hyperemia of the abdominal organs, but especially, marked thickening of the pleura and inflammatory infiltration of the lungs, generally leading to pronounced pulmonary fibrosis. The pulmonary changes will be discussed in another section. The cardiac abnormalities consisted in pericardial effusion, dilatation of the right auricle and ventricle, inflammation and degeneration of the cardiac cells, hyperemia of the interfibrillar capillaries, occasional hemorrhages, and leucocytic infiltration. Infarction of the right auricle and sulcus terminalis, and thrombosis of the tip of the auricular appendage, occurred in several dogs. An important finding was the marked thickening or actual obliteration of the blood vessels. Electrocardiographic studies of cardiac function presented an inversion of T waves in one or more leads, slight enlargement of the P waves in lead II, a moderate increase in the QRS complexes of leads II and III, occasional prolongation of conduction time, a subsequent increase in rate, and, in some instances, auricular flutter and fibrillation.

These experiments had been undertaken with the hope of finding a non-surgical method of inducing myocardial lesions and electrocardiographic abnormalities, and from this point of view they were entirely successful. But they can hardly be said to shed new light on the action of radiation on the heart. Most of the cardiac alterations observed could well have been the indirect result of the extensive inflammation of pleura and lungs, and, in some of the animals, of the kidneys and liver. The thickening or obliteration of blood vessels, however, was probably a direct and specific effect, because blood vessels are affected adversely even by doses of roentgen rays much smaller than those used in these investigations, although larger than those currently employed in the treatment of human beings. Such changes in the blood vessels may account, at least in part, for the hemorrhages in the substance of the auricle. The marked hyperemia of the kidneys and other abdominal organs of animals irradiated only over the thorax (unless the thoracic fields were sufficiently large to include the kidneys and liver), must necessarily be regarded as secondary to the marked pleuritis and pneumonitis, and to the circulation of toxic products of cellular disintegration, caused by the rays. Hartman, Bolliger, and Doub (1927) have submitted clear evidence that irradiation injury to the renal apparatus may cause a distinct functional and organic reaction of the heart. It is not difficult to conceive, therefore, that the cardiac changes also may have been secondary, and not direct and specific, effects of irradiation. The evidence furnished is not absolutely conclusive, but it appears likely that both a direct and an indirect influence combined to yield the abnormalities described; this is especially true if the vascular alterations are borne in mind. The experiments of Hartman, Bolliger, Doub, and Smith undoubtedly prove that the heart, like all other organs and tissues, can be injured by exposure to sufficiently large doses, but at the same time they serve to

confirm, and to increase our respect for, the exceptional ability of the heart to tolerate irradiation. It may be safely concluded, however, that the heart is not in danger of direct injury from doses of roentgen rays such as those ordinarily employed in radiotherapy, and that its only danger arises from its proximity to the more sensitive pleura and lungs. Since the tolerance of the heart to radiation is several times greater than that of the pleura and lungs, a dose of roentgen rays which the pleuro-pulmonary structures can tolerate is not likely to have any deleterious effect on the heart.

Many radiologists of large experience have never observed or reported clinical manifestations of cardiac disturbance imputable to irradiation, although, especially in connection with tumors of the breast, bronchus, and mediastinum, the heart of a large number of patients has been exposed to the direct action of large doses of roentgen rays. If the heart were as sensitive to irradiation as certain investigators have misleadingly inferred, presumptive or absolute clinical evidence of cardiac irritation or injury must be more abundant. The relative absence of such evidence can only mean that the heart possesses a high degree of resistance to direct irradiation or to the toxic factors of ordinary indirect irradiation. Providing the organ was organically and functionally sound before irradiation, the conclusion seems warranted, that unmistakable injury to the heart of a human being, following radiotherapy, must be regarded as an indication of gross excess in dosage, or of too concentrated treatment, and can hardly occur without even more obvious lesions in the skin, pleura and lungs, or other organs exposed to the rays.

Radium. The functional and organic action of radium or its derivatives has been investigated in several different ways. The experiments of Prime (1915) and of Goodrich and Scott (1925) on the effect of radium on the heart of chick embryos show conclusively that radium influences chiefly the mitotic division of the explanted cardiac cells and hence the growth of the tissue. This furnishes another example of the inhibition of growth induced by irradiation of embryonic cells or tissues. In the studies of Goodrich and Scott, the cultures were not carried beyond seventy-two hours, but during this time no change in the rhythmic contraction of the muscle cells could be discerned. Prime, who carried his cultures through as many as nine generations, found that, even among the explants in which growth ceased altogether, many continued to beat. Prime's conclusion that radium acts chiefly on the nuclear mechanism of cell division and not on the protoplasm seems well founded.

The investigation, by Fromme (1916), of the action of radium on the heart of frogs, axolotl, and mice appeared to show that the result of irradiation was fatty degeneration of the organ. As is well known, some measure of fatty degeneration of the heart is such a common finding after death from many different causes that it can hardly be accepted as a criterion of the direct effect of irradiation. Moreover, since the experiments with roentgen rays have shown that approximately equal degrees of fatty degeneration were found in unirradiated control animals as in those exposed to the rays, there does not seem to be much ground for the assumption that the fatty changes present in the heart after exposure to radium must be a direct and specific effect of such exposure. Rather, it must be concluded that such fatty transformation must have been either independent of irradiation, or only an indirect effect, either related to nutritional disturbances, or to the circulation of toxic prod-

ucts of cellular disintegration in sensitive structures, induced by irradiation. On scanning the experiments of Lazarus-Barlow (1922), however, there appears to be a more definite relationship between irradiation and at least some of the abnormalities noted. It is important to remember that the entire body of the animals was exposed to the gamma radiation emitted by 5 grams of radium, and that this resulted in extensive, degenerative alterations of the leucocytes in the circulating blood, spleen, lymph nodes, intestinal lymph follicles, and bone marrow, and also in some of the cells of the generative glands, stomach and intestine, kidneys, liver, lungs, and other organs. It would be surprising, to say the least, if such far-reaching effects should not have had any reverberations in the heart. The fact that the cardiac changes appeared to increase with the dose of radium does not vitiate this interpretation, because the more pronounced the changes induced in other organs, the greater must also have been the cardiac abnormalities. But a direct relation of irradiation and nuclear vacuolation and intermuscular extravasation of erythrocytes seems probable, though these also may have been indirect effects. Certainly, the results obtained by Lazarus-Barlow indicate that the heart is less sensitive to irradiation than many other organs and tissues, and agree, therefore, with the effect of exposure to roentgen rays.

It is not surprising that when Borman (1927) introduced radium emanation in small, sealed, glass tubes beneath the epicardium, in the region of the sino-auricular node, he should have found that the cardiac tissue in the vicinity of the tubes of radioactive substance had undergone degeneration. In sufficient doses, radium or its emanation is known to destroy all tissues within a certain radius from the source of radiant energy. Some tissues, it is true, are more sensitive than others, and degenerate more rapidly with the same dose, or equally with smaller doses, but Borman's reports do not furnish evidence that the sino-auricular node is more susceptible to irradiation than the adjacent cardiac tissue. His observation that the tissue of the sino-auricular node appeared more sensitive than the surrounding tissue may be well founded, or may rest on a possible difference in distance between the radioactive substance and the node and other cardiac tissue in question. The information furnished is not sufficient to establish clearly which of these two possible factors may have been responsible. For the same reason, it is impossible to be certain whether or not his deduction that the tissue of the node is embryologically more primitive is warranted. Borman's experiments furnish additional evidence of the relative sensitiveness of the blood vessels, which become engorged, degenerate, rupture, and subsequently undergo sclerotic thickening sometimes leading to obliteration. The studies of Coryllos, Edwards, and Bagg (1923) showed that doses of from 200 to 400 millicuries of radium emanation, applied directly to the auriculoventricular valves, caused an inflammatory reaction leading to scarring of the valves. This is in accordance with the well-known effect of insufficiently filtered radium at close range, and, under the circumstances, this effect might well have been predicted.

The experiments of Maass (1911), Maass and Plesch (1913), Zwaardemaker and Feenstra (1916), Zwaardemaker (1916), Zwaardemaker, Benjamins, and Feenstra (1916), Zwaardemaker (1917), Kemen and Kisch (1919), Zondek (1921), Fröhlich (1923), Viale (1923–24), Zwaardemaker and Zeehuisen (1924), Kawashima (1924), Zwaardemaker (1925), Zwaardemaker and Zeehuisen (1927), and Zwaardemaker and Feenstra (1928), all relate to the influence of radiant energy in the form of

radium emanation, thorium, mesothorium, uranium, or potassium on the intricate functional mechanism of the heart. It must be frankly recognized at the outset that any attempt to analyze the results of these several investigations may lead into the domain of romance. Perhaps no field of experimentation is fraught with more uncertainty and greater difficulty in the interpretation of results. The mechanism which governs the function of the heart is sensitive, and responds more or less quickly and in varying degrees, to the multitude of factors to which this major vital organ is constantly exposed. To analyze all these experiments in any detail would involve a review and discussion of the extensive experimental literature of the mechanism of the heart beat.

Maass, and Maass and Plesch, wisely hesitated to draw conclusions from the variable results of their studies on the influence of radium emanation and thorium X on the isolated heart of frogs. In their different experiments the behavior of the heart was so inconstant that, in the absence of more detailed information on certain points, such as the time the perfusing fluid was allowed to flow through the heart, it is impossible to account for the ensuing divergences of function. The transient fall in arterial pressure and minute volume, and the slight increase in rate after a dose of 40 electrostatic units of thorium X per cubic centimeter of perfusing solution might have continued longer, or even increased, had not this reaction been abolished by perfusion with plain Ringer's solution. In other experiments with smaller doses of radioactive substance, an increase in the minute and pulse volumes was accompanied by a slight decrease in rate. Maass and Plesch deduced that thorium X and radium emanation increase the diastolic distensibility of the heart, and that thorium X improves cardiac activity and lowers vascular resistance, but the evidence submitted by them is far from conclusive. Their investigation of the effect of thorium X on blood pressure has little, if any, value, but one feature of their experiments deserves attention. This is that some of the animals which had received injections of thorium X became prostrated, lost weight, and died, and at necropsy hemorrhages were found in the gastrointestinal mucosa, kidneys, and fasciae. Radioactive substances injected into the circulation are excreted largely through the gastrointestinal tract and kidneys, to which more or less severe injury may result from excessive doses. It would be reasonable to expect that some of the discrepancies in their findings may have been due to factors such as those indicated, and that the fall in blood pressure was a consequence of depression in vitality or metabolic activity. These considerations may also apply to the experiments of Tsiwidis, although to a less marked degree, but since no mention of tissue abnormalities from irradiation was made, the precise relation between the injected radioactive substance and the oscillations in blood pressure and variations in cardiac function must remain obscure.

The investigations of Kemen and Kisch, who used enormous doses of radium emanation, were essentially negative, so far as the influence of radium emanation on cardiac function is concerned. In a few instances, an initial acceleration was followed by a slight depression in cardiac activity, and arrhythmia, which disappeared promptly when the emanation solution was stopped, occurred in two cases; but similar disturbances of rhythm were noted in one case before the heart had been subjected to radioactive action, and, in this instance, the arrhythmia disappeared while the heart was being perfused with the emanation-Ringer's solution. Kemen and

Kisch undoubtedly were right in concluding, therefore, that intravascular doses, such as are used in treating human beings, probably have no injurious effect on the heart.

Zwaardemaker, alone or in collaboration with Feenstra, Benjamins, or Zeehuisen, carried out a long series of experiments. They assumed that, because the heart stops beating when potassium is removed from normal Ringer's solution, and because uranium, rubidium, thorium, and radium emanation may, in certain doses, cause the heart to resume pulsation, the influence of potassium and of the other chemicals mentioned must be due to their radioactive content. They postulate further that cardiac muscle contains a mother substance, which they suggestively designate as automatinogen and which, under the influence of the minute proportion of radioactive matter contained by potassium, is transformed into automatin; it is this product to which they ascribe the rhythmic action of the heart. The radiant energy emitted by potassium is known to be extremely slight. Nevertheless, as Scott has recently indicated, the small quantity of radiant energy emitted by potassium would not necessarily remove the possibility of its being sufficient to influence the delicate functional mechanism of the organ. But, as has been shown by the large number of experiments by many physiologists, cardiac function is affected by minute variations in the chemical, thermal, and other factors acting on it. Other factors probably exert a more or less important action on cardiac rhythm, and it is possible that radiant energy also may have a definite influence. Still, the results obtained by Zwaardemaker and his associates are not conclusive, and the possibility that the effects described may have an ionic rather than a radioactive basis has not been excluded. Final appraisal must be reserved until further study has brought sufficient confirmatory or conflicting evidence to throw more light on the problem.

Viale (1923–24) was unable to confirm the deductions of Zwaardemaker and his coworkers. For instance, Viale found that potassium almost always had a negative inotropic and chronotropic action; uranium, a positive inotropic and a negative chronotropic action; and thorium, a positive chronotropic action, in spite of the fact that both uranium and thorium emit the same radiations. Viale thought that Zwaardemaker's so-called "paradoxical phenomenon" was due to a modification in the colloids of the heart, because a similar phenomenon occurred whenever the composition of the perfusing solution was changed, such as when a solution of sodium chloride was substituted for serum. Zondek (1921) repeated the experiments of Zwaardemaker and his pupils, but was unable to duplicate their results, and concluded that the action of potassium on the heart has nothing to do with radioactivity. Fröhlich (1923) also found that perfusion of the heart of frogs and rats with Ringer's solution containing radium emanation, or allowing such a radioactive solution to drip on the sinus and ventricles, caused the organ to resume the regular and approximately normal pulsation which had been diminished in quality and frequency by having been kept at a low temperature for from three to twenty-four hours, by having been perfused with unwarmed blood, or with Ringer's solution and grape sugar at 20° C., to which defibrinated blood has been added. Fröhlich's results indicate that small doses of radium emanation may stir a sluggish or irregular heart to renewed activity, but it is not clear whether this is a true radioactive effect, or whether the functional recovery may have been due to the inter-

rupted action of the factors responsible for the previous inhibition and irregularity of the heart. Moreover, Fröhlich did not state how soon after the beginning of perfusion with radium emanation these effects appeared, and how long they lasted. He could not agree with Zwaardemaker, and thought that the action of potassium is due to specific ions, while that of radium emanation is atomic in character, and involves a destruction of energy. Kawashima (1924) failed to observe any effect of a mixture of thorium emanation and oxygen, made to flow through the isolated heart of frogs.

Whether the effects on the heart of potassium, uranium, rubidium, thorium, and radium emanation are to be attributed to ionic or radioactive factors, or to modifications in the cardiac colloids, or whether Fröhlich's contention that the action of potassium is ionic, while that of radium emanation is atomic in character, is to be accepted, it is clear that the intricate problem of the rhythmic function of the heart and of the multiple factors which may influence it is far from settled.

To be Continued.